DECEMBER, 1933.

BRAIN.

PART 4, VOL. 56.

POSTURAL RELATIONS OF THE FRONTAL AND MOTOR CORTEX OF THE DOG.[1]

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THE control of posture by the central nervous system has remained the subject of continual study since Sherrington (1896) made his original and stimulating observations on the phenomenon of decerebrate rigidity. A review of the literature (Langworthy, 1928) shows that numerous investigators have sought to determine the centres and pathways responsible for the maintenance of this condition and to discover the source of the influences which normally modify or inhibit it. Such a review makes it evident that the nervous control of posture is a very complex matter involving many levels of the nervous system from the local spinal reflex arc to the cerebral mantle itself. It is the relationship of the cortical level which concerns us here.

Recent studies have offered a conflict of opinion as to the area of the cortex actually involved in postural control. The work of Warner and Olmsted (1923), Olmsted and Logan (1925), King (1927) and Langworthy (1928), supports the view that profound changes of a postural nature, resulting from lesions about the cruciate sulcus in cats, occurred only when the inexcitable area frontalis was destroyed. Lesions limited to the excitable zone produced flaccid paralysis without extensor phenomena. On the other hand Laughton (1928), working with guinea-pigs, rabbits, cats and dogs, McKibben (1929), McKibben and Wheelis (1932) and Bard (1933), using cats, have failed to confirm those results and conclude that extensor rigidity

[1] This work was done while the author was a Fellow of the Henry Strong Denison Medical Foundation.

and its associated phenomena always follow the destruction of the excitable area itself.

In view of this divergence of opinion it was thought that additional data might confirm the work of one or the other of these groups, or perhaps correlate the views of the two. Since the cat has been used for the major portion of previous studies, a comparative study was projected for the dog, for in that animal's brain the areas with which we are concerned are larger than the homologous regions in the cat. This paper presents the physiological observations made on thirty-two dogs, from which various portions of the frontal and motor areas of the cortex were removed. The evidence obtained supports the thesis that postural phenomena are associated with destruction of the excitable area of the cortex. A study of the cyto-architecture of the areas ablated and of the degenerations produced by certain of the lesions will form the subject of a later report.

Methods.

The experiments were controlled not only by a preliminary histological study of the cortex, but also by delimitation of the excitable area with a unipolar electrode. This electrode carried either induced current from a secondary coil, or a 60-cycle alternating current from the house circuit reduced to voltage values variable between 2 and 5 volts.

Operations were performed aseptically under full surgical anæsthesia induced either with ether by inhalation or with nembutal (Abbott) given intra-peritoneally. 25 to 40 mgm. of the latter drug per kilogram of body-weight gave surgical anæsthesia lasting from two to four hours with a threshold of electrical stimulation lower than occurred under ether. (*Cf.* Keller and Fulton, 1931; Fulton and Keller, 1932.)

The animals were kept under observation after operation for periods of time varying from a few weeks to several months. Then they were killed by anæsthetics and the brains fixed with 10 per cent. formalin injected through the heart, preceded by warm normal saline to wash out the vessels. The extent of the actual lesion in each case was carefully determined after removal of the brain from the skull.

Experimental Observations.

1.—The Extent of the Electrically Excitable Cortex of the Dog.

Electrical stimulation showed that the excitable motor area was localized to the lateral third of the anterior and the whole of the posterior sigmoid gyrus (fig. 1). The gyrus proreus and the medial half

to two-thirds of the anterior sigmoid were found to be silent; so also was the cortex lateral to the coronal fissure.

Well-defined movements of the contralateral facial muscles were obtained upon stimulating points of the cortex in the outer third of the anterior sigmoid. Excitation of the anterior gyrus as it began to swing around the end of the cruciate sulcus produced contralateral flexion of the neck. As the exploration was carried to the posterior gyrus isolated flexor movements of the fore-leg appeared, usually of the whole limb but sometimes of its segments. Occasionally movements of extension

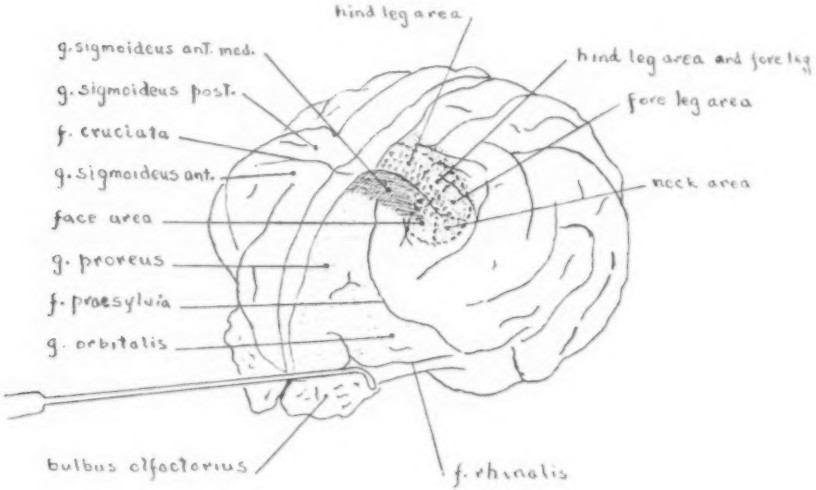


FIG. 1.—Drawing of fore-brain of the dog, after a photograph, showing the excitable area, the histological fields about the cruciate sulcus, and the extent of the inexcitable frontal area. The Betz-cell area is indicated by small triangles; granular cortex by fine stippling; agranular cortex is cross-hatched.

occurred. When about one-third of the length of the posterior gyrus had been traversed, stimuli produced simultaneous flexion of the fore- and the hind-leg. From the medial half, together with the medial surface of the posterior sigmoid, movements of the hind-leg were obtained.

Examination of both hemispheres in the same animals showed no appreciable variation in the distribution of cortical motor points.

If the strength of stimulus was properly controlled no reaction resulted when areas outside those just described were stimulated. However, if, after exciting a point in the motor area, another lying

within a short distance but outside the excitable area were stimulated, the phenomenon of facilitation could be demonstrated.

Histological study showed that the area responding to electrical stimuli extended beyond the distribution of the typical Betz-cells to overlap the sensory granular cortex posteriorly and an agranular type, similar to Brodmann's Area 6, anteriorly. This is important to bear in mind in drawing conclusions from the ablation experiments.

II.—The Effects of Ablations in the Frontal and Motor Areas.

As a result of differential ablations it was found that lesions located entirely anterior to the electrically excitable area produced no demonstrable effects, but as the excitable zone became involved alterations began to appear which reached a maximum when the entire responsive area was destroyed. It will be convenient first to indicate the experiments which led to this conclusion, and then to describe in some detail the results of effective cortical ablations.

TABLE I.

Animal number	Extent of lesion
1.	G. proreus and adjacent medial surface, L.
2.	,, ,, ,, ,, ,, ,, ,,
3.	,, ,, ,, ,, ,, ,, Bilat.
4.	,, ,, ,, ,, ,, ,, ,,
5.	G. proreus and coronal tip, L.
6.	,, ,, ,, ,, ,, Bilat.
7.	G. proreus, adj. med. surface, g. orbitalis, L.
8.	,, ,, ,, ,, ,, ,, ,, ,,
9.	1st op., g. proreus, adj. med. surface, g. orbitalis, L. 2nd op., g. proreus, g. sigmoid., R.
10.	1st op., g. proreus, adj. med. surface, g. orbitalis, L. 2nd op., g. sigmoid., Bilat.
11.	G. proreus, adj. med. surface, g. orbitalis, Bilat.
12.	G. proreus (upper one-third), Bilat.
13.	G. proreus, coronal tip, g. sigmoid. ant., Bilat.
14.	,, ,, ,, ,, ,, ,, ,, ,,
15.	,, ,, ,, ,, ,, ,, ,, ,,
16.	,, ,, ,, ,, ,, ,, ,, ,,
17.	,, ,, ,, ,, ,, ,, ,, L.
18.	1st op., g. sigmoid., L. 2nd op., g. proreus, g. sigmoid., R.
19.	G. sigmoid., L.
20.	,, ,, ,,
21.	G. sigmoid, ant. (med. two-thirds), L.
22.	G. sigmoid, ant. (med. one-half), and adj. med. surface, L.
23.	,, ,, ,, ,, ,, ,, ,, ,, ,, ,,
24.	1st op., g. sigmoid. ant. (med. one-half), and adj. med. surface, L. 2nd op., g. sigmoid. ant. (lat. one-half), g. sigmoid. post. (lat. two-thirds), R.
25.	1st op., g. sigmoid. ant. (med. one-half), adj. med. surface, Bilat. 2nd op., g. sigmoid. ant. (lat. one-half), g. sigmoid. post. (lat. one-half), L.
26.	G. sigmoid. ant. (lat. one-half), g. sigmoid. post., L.
27.	,, ,, ,, ,, ,, ,, ,, ,, ,,
28.	,, ,, ,, ,, ,, ,, ,, ,, ,,
29.	,, ,, ,, ,, ,, ,, ,, ,, ,,
30.	,, ,, ,, ,, ,, ,, ,, ,, ,,
31.	G. sigmoid. post., L.
32.	,, ,, ,, and a portion of sensory cortex, L.

(1) *Lesions of frontal areas anterior to excitable cortex.*—By reference to fig. 1 and Table I, the situation and extent of the lesion in each animal can be determined. The region anterior to the sigmoid gyrus includes (1) that portion of the coronal gyrus lying anterior to the sigmoid gyrus above the presylvian fissure, which may be conveniently designated the coronal tip; (2) the gyrus proreus down to the olfactory bulb, together with the adjoining medial surface; and (3) the orbital gyrus which extends infralaterally between the presylvian and rhinal fissures. Lesions of various extent were made in this region in 12 animals (1-12), unilaterally in 7, bilaterally in 5. Negative results were obtained in each case, except for an increase in general motor activity in 3 and 5. This type of alteration was seen in other animals (*vide infra*, 15, 10, 27). Since its occurrence bore no constant relation to the site of the lesion the explanation for it seems to lie rather in technical procedures, although this cannot be proved.

(2) *Lesions of anterior areas encroaching upon excitable cortex.*—In five animals (13-17) lesions of the anterior areas extended backward to involve almost completely the anterior limb of the sigmoid gyrus. Four of these cases were bilateral, the other was a unilateral ablation. No sensory or motor symptoms occurred in the first three animals except for a rather marked hyperactivity in 15. Dogs 16 and 17, however, presented distinct sensory and motor disturbances, consisting of altered sensitivity to pin prick, uncorrected postures of the legs, extensor rigidity and difficulty in the use of the limbs. Considerable hæmorrhage occurred at operation in 17 and this animal showed gross contralateral weakness for the first half week. Symptoms persisted in 16 until the animal was sacrificed (four weeks), but in 17 they disappeared after one month. In the latter case the posterior sigmoid in its middle portion was involved in adhesions.

(3) *Lesions destroying the entire sigmoid gyrus.*—In five cases the entire sigmoid gyrus was removed with striking results. In animal 9, which previously had had the left gyrus proreus and the orbital gyrus removed without effect, a right-sided lesion was made which included the gyrus proreus and the entire sigmoid gyrus. In 18, 19 and 20 the lesions were limited to the sigmoid gyrus on the left. After one week the gyrus proreus and the gyrus sigmoideus were removed from the right hemisphere of 18. The sigmoid gyrus of dog 10, from which the left gyrus proreus and the gyrus orbitalis had been removed earlier (*vide supra*), was destroyed bilaterally. Maximal changes, which will be considered in detail below, occurred in these animals. Two of the

animals (19 and 20) showed rather marked contralateral weakness for the first few days after the operation. Since these were the only two cases, except for 17, which showed this degree of weakness, it may be well to remark that in all three of these animals bleeding was considerably greater than in any others of the whole series.

(4) *Partial ablations of the sigmoid gyrus:* (*a*) *Lesion of the anterior sigmoid.*—Partial ablations of the sigmoid gyrus were next undertaken to determine what portion of it was responsible for the clinical phenomena produced. The evidence already obtained indicated that the anterior sigmoid could be destroyed almost completely without effect, though this was not true in all cases. Therefore the left anterior sigmoid alone was removed from one animal (22). No response to electrical stimulation was obtained except at the very lateral end of the gyrus and this part was not included in the lesion. Very mild symptoms lasting three weeks followed this ablation. At autopsy about two-thirds of the posterior sigmoid gyrus was found elevated and roughened by adhesions.

(*b*) *Lesions of the medial half of the anterior sigmoid.*—In four animals the medial half of the anterior sigmoid, together with the adjacent medial surface, was carefully destroyed. This was done with minimal hæmorrhage since it was not necessary to sever any large blood-vessel. In three of the cases (22, 23 and 24) the lesion was limited to the left side; in the fourth (25) it was bilateral. None of these animals ever developed any signs of sensory or of motor defect, although they were subjected to detailed examination repeatedly.

(*c*) *Subsequent lesions of the excitable cortex in animals of group* (*b*). —In two of these cases subsequent lesions of the electrically excitable area were made. The lateral third of the anterior and the lateral two-thirds of the posterior sigmoid were removed from the right hemisphere of 24. The lateral halves of the left anterior and posterior sigmoid were destroyed in 25. Typical alterations occurred after these lesions, though they were not as severe as in the total destruction of this gyrus. Furthermore, in 25 the resulting physiological changes affected chiefly the contralateral fore-leg—a finding in consonance with the fact that the cortical area of the hind-leg was left intact.

(*d*) *Lesions of the excitable cortex alone.*—From five animals (26-30) the electrically excitable area was removed by destroying the lateral half of the anterior and the whole of the posterior sigmoid gyrus. Each of these dogs developed in a pronounced manner the same clinical features which characterized those animals from which the entire sigmoid gyrus was excised. Not one of them showed a flaccid paralysis. Every

one of these animals could stand, walk and even run as soon as the effect of the anæsthesia (ether) wore off.

(e) *Lesions of the posterior sigmoid.*—Practically the same effects were produced by destroying the entire posterior sigmoid alone in one case (31), and the posterior sigmoid plus a portion of the cortex directly behind it in another (32.)

From these experiments it is evident that lesions entirely anterior to the electrically excitable area were not associated with the appearance of clinical manifestations, but that symptoms did appear when the excitable area became involved and were maximal when the entire responsive area was destroyed. The typical alterations produced by effective lesions will now be described.

Many deviations from the normal were found in these animals, both when they were observed during spontaneous activity and when they were subjected to special test performances. Changes were always contralateral to the lesions and were easily demonstrable in unilateral cases by comparison with the unaffected side. Marked weakness occurred in but three cases, as noted. All others could stand, walk, or even run as soon as the anæsthesia wore off. Stiffness of the affected limbs was noted in some animals, but usually progression was fairly normal except for moderate inco-ordination. Footing was insecure on a smooth surface, so that slipping frequently, but falling seldom, occurred. Paws often were left dorsum to the ground, and limbs assumed abnormal postures of adduction, abduction, ante- and retro-position. Similarly, such positions might be passively imposed and remain uncorrected until some spontaneous activity required the use of the part. Animals accustomed to climbing stairs had difficulty in doing so after operation through failure of the affected limbs to clear the steps readily.

In all cases well-marked contralateral extensor rigidity was easily demonstrable. This became evident when the animal was lifted in a horizontal position above the floor, and was best seen when a hammock was used for support (Plate XII, figs. 2 and 3). For while the ipsilateral limbs flexed, rigid extension engaged both contralateral legs at all joints, including ankle and wrist, and the toes fanned. Passive flexion was resisted, and during the first week post-operatively there resulted a spring-like rebound when the foot was released after passive flexion of the wrist. The limb as a whole gave way with "jack-knife" suddenness to pressure applied at the sole. Rigidity was likewise apparent when the animal was held back-to-examiner (figs. 4, 5, 6). In either the ventral or the vertical position the fore- and the hind-legs seemed equally hyper-

tonic, but when the animal was placed on its back the fore-leg alone was usually affected (fig. 12). In some cases spontaneous extension did not occur at all in the dorsal position, or, if it did, the limbs flexed when the animal became quite quiet. However, a difference in the extensibility of the limbs of the two sides could be demonstrated by gently pushing the hind-legs caudalward with pressure applied just above the knees, or by forcing the fore-legs forward by pressing just above the elbows. All four limbs were thus passively extended, but the angle through which one had to move the limbs to produce extension was much less on the affected side than on the unaffected one (fig. 13). The difference in rigidity could also be demonstrated by grasping the animal about the thorax and gently swinging it so that a pendular movement was imparted to the limbs, particularly the fore-limbs. The ipsilateral fore-leg alternately flexed and extended at all joints, including the wrist, as the limb swung backward and forward respectively. The contralateral one, however, moved as a rigidly extended whole, and flexion failed to occur.

In most of the cases a further feature was evident when the animal was held in the back-to-examiner position. There was extreme flexion of the animal's neck and trunk to the contralateral side and slightly forward (fig. 11). If an attempt were made to correct this position by straightening the body a marked resistance was encountered. This hypertonicity of the trunk muscles was emphasized by holding the animal in a lateral position with the side parallel to the ground. A normal animal attempts to right itself and produces a concavity of the body upward, whichever side be held toward the ground. But in these animals, when the side contralateral to the lesion was toward the floor, there was a marked concavity downward (fig. 10), and when the contralateral side was up the normal upward concavity was greatly accentuated (fig. 9). Hypertonicity and resistance to lengthening of the trunk musculature have not previously been described in association with experimental cortical lesions.

Typical difficulties were noted in the animals' ability to use their limbs. These were especially evident in the usual escape efforts which are made when an animal is held. Immediately after operation only the ipsilateral limbs took part in these movements; the contralateral ones remained quite still. A few days later attempts at movement were made on that side, but the limbs tended to move as rigid wholes from the proximal joints. Although improvement occurred, the difficulty continued for months. This "paralysis" of movement was well

shown when the animal tried to get out of the hammock (fig. 8). The ipsilateral limbs were readily extracted from the holes through which the legs passed, but the contralateral ones could be withdrawn only with the assistance of the ipsilateral members. This inability to extricate the limbs and place them beside the body is a failure of one of the placing reactions of Rademaker (1931) and Bard (1933). Investigation revealed that other placing reactions were also absent. Thus when the non-blindfolded animal was moved toward a table edge, a visual placing reaction was elicited as soon as the dog was near enough to place the foot upon the table (fig. 16). Only the ipsilateral one was so placed. If the animal was prevented from seeing the table and the backs of the fore- or hind-paws were touched to the edge the ipsilateral limb at once was placed upon the table (figs. 17, 18, 20, 21). The contralateral one failed to react until backward displacement by pressure against the table supplied an added stimulus. Likewise after the chin was brought in contact with the underlying surface while the fore-legs were held down, only the ipsilateral paw was placed beside the jaw when the limbs were released (fig. 19).

Other differences, comparable to the disturbances of the hopping reactions seen after similar lesions in cats (Bard), were noted in the use of the legs in all cases. When a normal dog is made to stand erect on its hind feet it steps back with both legs to correct to the all-fours position. After the excitable area had been destroyed on one side the contralateral limb failed to show this reaction; the ipsilateral one alone stepped back with a tendency to execute a circle about the other foot, which remained firmly stationed as a pivot. If instead of being held in one position, the dog were caused to walk forward in the erect attitude the ipsilateral leg stepped in a normal manner; the contralateral one dragged along in hemiplegic fashion, usually with toes turned under, or at times it would move with infrequent, reluctant steps. Likewise the contralateral limb failed to correct its position upon lateral displacement of the body (fig. 24).

Similar defects were demonstrated in the fore-leg by causing these dogs to walk on the fore-legs alone. The normal one stepped readily; the affected one did not, with the result that pivoting occurred about the contralateral foot. When the animal walked backward on its front legs the normal limb performed stepping movements; the abnormal one failed to do so and slid medially toward the ipsilateral side (fig. 14).

One other reaction may be noted here. If, while standing on all four legs, one of these animals was lifted off the floor, even though great

care was taken to lift the animal evenly as a whole, the contralateral feet left the floor before the ipsilateral ones did, and became elevated above it an inch to an inch and a half before the ipsilateral ones left it (fig. 22). In returning, the ipsilateral feet were the first to touch the surface, as if reaching out for it.

Crossed extension reflexes could be elicited readily from the contralateral fore and hind limbs by a painful stimulus, or pressure to the corresponding foot pad, or by passive movement of the whole normal limb. Repeated passive flexion and extension of the ipsilateral leg often resulted in a gradual increase of extensor tone in the contralateral limb which finally produced a rigidly extended extremity (fig. 15).

The contralateral tendon-jerks were hyperactive, and alterations in the normal reactions to stimuli of deep pressure and of prick were also found on the side opposite to the lesion.

The clinical condition of the animals improved with the passage of time. But even months later all changes could be demonstrated in a a lessened degree. The photographs of animal 30 were taken two months after operation. The same phenomena were equally present when the dog was sacrificed two and one-half months later. In other cases this was true when they were killed seven months after operation. In some, however, reactions were nearly normal after two months. The hopping reactions apparently recovered most, but there was also a decrease in the extensor rigidity. The extensor attitude persisted: the resistance to passive flexion tended to disappear.

Discussion.

It has been possible in chronic experiments on dogs to show a correlation between the destruction of the excitable motor cortex of this animal and the occurrence of certain clinical phenomena of a postural nature. The excitable cortex was outlined by electrical stimulation. Lesions entirely anterior to this area failed to produce alterations in the sensori-motor reactions of the animals; but as the motor cortex became involved disturbances began to appear which became maximal when the entire excitable area was removed. The alterations were no greater when the motor area and all cortex anterior to it were destroyed than when the motor area alone was ablated.

The motor cortex of the dog, as outlined by electrical stimulation, is limited to the lateral third of the anterior sigmoid and the whole length of the posterior sigmoid gyrus, together with its medial extension for about two-thirds the width of the gyrus. This tends to agree with the

initial findings of Fritsch and Hitzig (1870). Slightly more of the anterior sigmoid responded to stimulation than gave origin to the cortico-spinal tracts in the dog studied by Holmes and May (1909). Our experience indicates that in the dog there is an orderly representation of contralateral movements from the face, through the neck and fore-leg to trunk and hind-leg, beginning in the outer third of the anterior sigmoid and continuing around the end of the cruciate sulcus to include the entire posterior gyrus. This agrees with the findings of Smith (1933) which have just been reported. There is no evidence in the dog of centres for the facial and neck musculature in the gyrus proreus corresponding to the findings of McKibben and Wheelis (1932) for the cat, which also are not supported by Langworthy's histological studies. The position of the face centre in the dog corresponds approximately with that reported for the cat by Weed and Langworthy (1926). The hind-leg areas of these two animals also correspond. But the fore-leg centre of the dog occupies a lateral position in the posterior sigmoid corresponding to their area D, which was inexcitable and did not have, in the cat, the characteristic structure of motor cortex. In the cat the fore-leg centres are medial to the face centres in the anterior sigmoid (Weed and Langworthy, 1926; Langworthy, 1928).

Unilateral destruction of the excitable motor area of the dog gave the following clinical phenomena: (1) The contralateral limbs assumed extended postures when the animal was held off the floor, suspended in a hammock or held with back to the examiner, and there was resistance to passive flexion in the extended limb. Rigidity might also be demonstrated, especially in the fore-leg, when the animal was on its back. (2) A similar hypertonicity affected the contralateral trunk musculature, resulting in a concavity of the body to that side when the animal was held in test positions, and there was resistance to passive straightening. (3) Weakness and inco-ordination affected the contralateral side. Usually the weakness did not amount to flaccid paralysis and the animal could stand, walk or run immediately after emerging from the anæsthesia. (4) Abnormal positions of the feet and limbs occurred spontaneously or might be passively imposed. These were not corrected until spontaneous movement required the use of the part. (5) There was failure to use the contralateral limbs in such movements as efforts to escape and in stepping backwards when held erect on the hind legs. Examination of these difficulties revealed that the hopping and placing reactions were deficient. (6) When the animal was lifted off the floor the contralateral limbs left first. (7) Crossed extension reflexes occurred

in the contralateral limbs to stimuli applied to the ipsilateral members. (8) The contralateral tendon reflexes were hyperactive. (9) There was impairment of superficial and deep sensibility.

All these alterations occurred contralaterally to the lesion and in no animal was the ipsilateral side affected. They were greatest immediately after operation and gradually decreased in severity until after several weeks many animals seemed quite normal. In others the deficiencies continued for months.

It is evident that the occurrence of extensor rigidity in association with lesions of the motor cortex does not agree with the view, derived from experiments on cats, that destruction of the area frontalis produces this effect. Clinically it is well known that rigidity occurs in association with pyramidal tract lesions in man. The similarity of hemiplegic spasticity to decerebrate rigidity has been stressed by Walshe (1919, 1923, 1929), who believes that the two conditions are physiologically identical although the former is but a fractional expression of the latter. This analogy was noted also by Riddoch and Buzzard (1922). However, the fact that capsular lesions produce greater spasticity than cortical motor lesions has suggested (Walshe 1919) that something more may be involved in the former than mere interruption of the pyramidal fibres. Actually it may mean a more complete lesion of the cortico-spinal fibres in the capsule or the interception of additional pathways. Those who hold that destruction of the area frontalis is responsible for the appearance of rigidity deny that the pyramidal tract plays any part. In this connection and confirmatory of the results presented here, it is interesting to note that Ranson, Muir and Zeiss (1932) studied the occurrence of extensor rigidity following spinal cord lesions in cats and concluded that in this animal, as in man, the cortico-spinal tracts convey impulses which inhibit extensor tonus. This has been confirmed for the dog and the cat by Tower (unpublished) who sectioned the pyramid from the ventral surface. Langworthy (1928) on the other hand sectioned the decussation of the pyramids in the sagittal plane from above and obtained flaccid paresis.

The premotor area of the hemisphere entered as a factor for consideration in tone distribution with the observations of Wilson and Walshe (1914) on "tonic innervation," of Adie and Critchley (1927) and of Critchley (1930) on forced grasping and groping in association with tumours and vascular lesions of this area. But how these disturbances may be related to what is usually thought of as pyramidal spasticity is not clear. Forced grasping and groping in man disappear when the

cortico-spinal tracts become completely involved and spasticity is maximal.

Richter and Hines (1932) were able to reproduce experimentally "forced" grasping in monkeys by removing Brodmann's Area 6. They were unable to demonstrate any associated spasticity. Study of the relationship of Areas 4 and 6 in monkeys (Fulton, Jacobsen and Kennard, 1932) showed that forced grasping without spasticity occurred after lesions of Area 6, and that flaccid paralysis resulted when Area 4 was destroyed. A combined lesion of the two however (Fulton and Kennard, 1933) produced the grasp reflex with marked spasticity, showing that unlike the situation reported for man the grasp reflex was not abolished by destruction of the motor cortex, and suggesting that for the appearance of spasticity the lesion must affect Areas 4 and 6 simultaneously.

In man circumscribed lesions of the Betz-cell area have not been made. The nearest approach was that of Horsley (1909) who removed all the cortex of the precentral gyrus from which electrical excitation produced movements in the corresponding arm. Our present knowledge of the structure (Brodmann, 1909; Vogt and Vogt, 1919; Economo and Koskinas 1925), and the excitability (Foerster, 1931) of this portion of the cortex makes it certain that the lesion Horsley produced included not only Area 4 but also Area 6. It would be important to know if a lesion of Area 4 alone would produce the same spasticity.

What have we learned in dogs of the relation of cortical areas to the occurrence of spasticity? It has not been possible to confirm the view that spasticity results when the inexcitable frontal areas are destroyed. Lesions of this region in the dog produced no effect. On the other hand when the excitable zone became involved symptoms began to appear which were maximal when the entire stimulable cortex was removed. A solution of the difficulty of correlating the findings of various workers may lie ultimately in a further analysis of the excitable area. For the motor cortex as outlined electrically in the dog extends beyond the distribution of the Betz-cells. In the frontal lobe of the dog studied histologically the medial third to half of the anterior sigmoid gyrus, which is not electrically excitable, is characterized by an agranular type of cyto-architecture similar to Brodmann's Area 6, while all the remainder of the frontal lobe of the dog's cortex is of the typical granular variety. Further, although the remainder of the anterior sigmoid gyrus and the whole of the posterior sigmoid gyrus are susceptible to electrical stimulation with low current strengths, the total

areas do not possess the typical cyto-architecture of the motor cortex. In the anterior sigmoid gyrus a short distance anterior to the crest of the cruciate sulcus the cortex is similar to Brodmann's Area 6, while the posterior division of the posterior sigmoid gyrus is characterized by the appearance of layer IV. However, in the depth of the cruciate sulcus, with the exception of the medial non-excitable cortex of the anterior sigmoid and of that forming the wall of the most lateral part of the posterior, the cortical mantle contains the large pyramidal cells of Betz in the fifth layer.

Although the experiments reported in this paper have taken cognizance of the cyto-architecture of the non-excitable medial division of the anterior sigmoid, it is practically impossible to differentiate previous to experimental ablation the exact limit of the motor cortex anteriorly in the anterior sigmoid and posteriorly in the posterior sigmoid, because the excitable area overlaps slightly the agranular Area 6 anteriorly and the granular area posteriorly. However, since most of Area 6 was destroyed by lesions of the medial half of the anterior sigmoid gyrus without effect, and since the same area was left intact with the production of maximal effects, it seems that Brodmann's Area 6 can have little to do with the production of spasticity in the dog. It, therefore, appears that cortical rigidity in this animal is a release phenomenon from the true Betz-cell area.

Extensor rigidity is but one of the manifestations of lesions destroying the excitable cortex of the dog. The question arises as to what relation the rigidity may have to these other disturbances. We may note that no one has described the occurrence of rigidity "in pure culture." Langworthy observed uncorrected postures of the legs, failure of the limbs to take part in escape efforts and alterations in superficial and deep sensitivity. He felt that these difficulties in postural adjustment and heightened threshold to sensory stimuli could well be explained on a basis of the rigidity. Bard, in his study of abnormalities of posture after lesions of the sensori-motor area in cats, came to the conclusion that the difficulties of adjustment were due to deficient hopping and placing reactions. He raised the question as to whether or not the rigidity might explain the difficulties, and decided in favour of the negative. For the rigidity was found to vary and at times was absent, while the deficiency of the placing and hopping reactions remained unchanged. Moreover, Brooks (1933) found in the rat that these reactions were disturbed without the appearance of rigidity.

There are still two conceptions possible regarding the relationship

of the rigidity to the associated phenomena. Either there is no causal connection and each is due to the destruction of separately functioning structures, or both result when the reflexes mediated through the destroyed centres are lost. As to the former, we may simply say that the separation has not yet been made. The view suggested here is that the rigidity appears because the reflex mechanisms of this level have been abolished.

Since many of the associated phenomena, such as the failure to correct abnormal postures or to respond properly to nociceptive stimuli, are distinctly of a sensory defect character, the sensory element must be considered. Whether these are actually the effect of sensory lesions or merely result from destruction of the efferent arc would be difficult to say. That all the symptoms may be due to a pure motor lesion is supported by experimental evidence that the entire symptomatology, as described in this paper, can be produced in cats and dogs by section of the pyramid in the medulla from the ventral surface (Tower, unpublished). However, Dusser de Barenne (1916) has shown for the cat that the sensory area overlaps the motor. This seems to be true for the dog also (Brown, unpublished), as was held by earlier workers on the cortex of this animal (Luciani, 1915). If these facts are true, it is impossible to destroy selectively either the motor or sensory area in these animals. Even in man Horsley (1909) found that sensory, particularly proprioceptive, changes occurred after destruction of the motor arm area. And in the macaque Dusser de Barenne (1924) showed a similar overlap.

It is therefore necessary to think of these experimental "motor" lesions as a combination of sensory and motor elements, and of their effects as losses of reflexes which pass through the centres destroyed. The difficulties of correcting posture are true defect phenomena. The rigidity, however, is a positive manifestation due to release of lower centres from cortical control. This control is not exercised by separate but by the same cortical centres that are involved in carrying out the reflexes which have been lost.

It is probable that in decerebrate rigidity there is a release of lower centres from several inhibitory centres of which the motor cortex, or the sensori-motor cortex, is but one. This view has been stressed in the recent papers of Ranson and his colleagues who have been able to show various degrees of rigidity according to the level of transection of the brain-stem (Ranson and Hinsey, 1929A; Hinsey, Ranson, McNattin, 1930; Windle, 1929). Can a general correlation be made between the

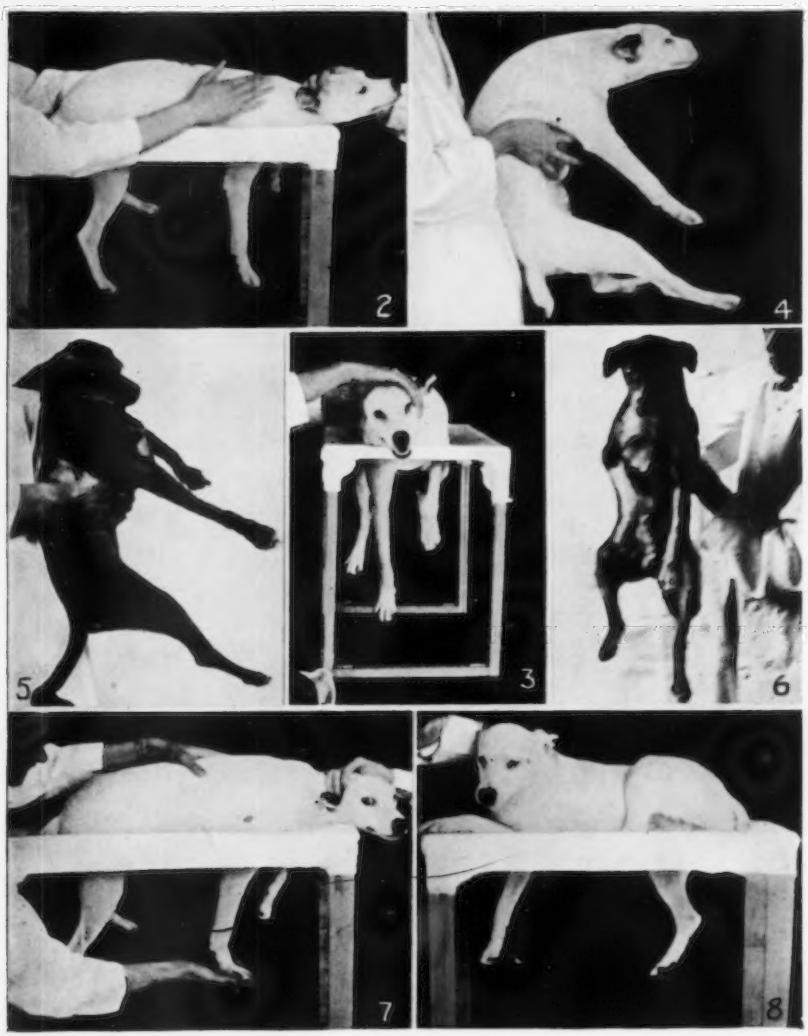
occurrence of rigidity and the destruction of centres which normally permit the animal to adjust itself to its environment through movements of righting, progression, placing and hopping, and the like? The evidence is by no means conclusive, but it is suggestive of such a possibility. Such an interpretation is consistent with, and indeed, suggested by, the conception already current concerning decerebrate rigidity and its relation to progression. Movement and the extensor attitude are reciprocal phenomena. The latter is inhibited during movement and appears, when the tone-maintaining centres are still intact, after the mechanisms presiding over movement have been destroyed.

Summary.

From thirty-two dogs various areas of the motor and frontal cortex, controlled histologically and by electrical stimulation, were removed. The animals were studied for periods varying from a few weeks to several months. Lesions entirely anterior to the excitable area failed to produce effects. As the excitable area became involved symptoms appeared which were maximal when this area alone was ablated. These changes were entirely contralateral and consisted of extensor rigidity and resistance to passive flexion in the legs; a similar hypertonicity of the trunk musculature resulting in concavity to that side with resistance to passive straightening; uncorrected postures of the extremities; failure of placing and hopping reactions; crossed extension reflexes; hyperactive tendon reflexes; decreased superficial and deep sensitivity. There was no true flaccid paralysis.

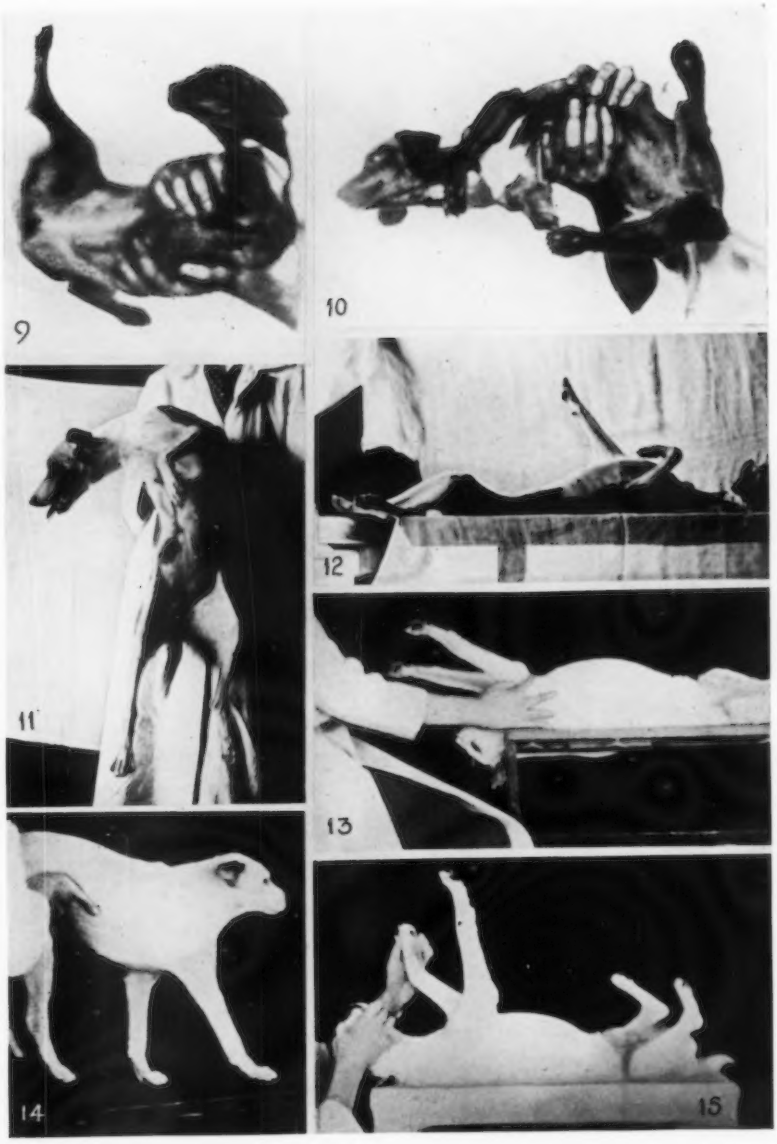
The total area susceptible to electrical stimulation did not possess the typical structure of motor cortex. Anteriorly it overlapped an area similar to Brodmann's Area 6. Posteriorly layer IV appeared. The evidence indicates that removal of Area 6 does not produce spasticity in the dog. Rather rigidity results when the motor or sensori-motor area is destroyed.

PLATE XII.



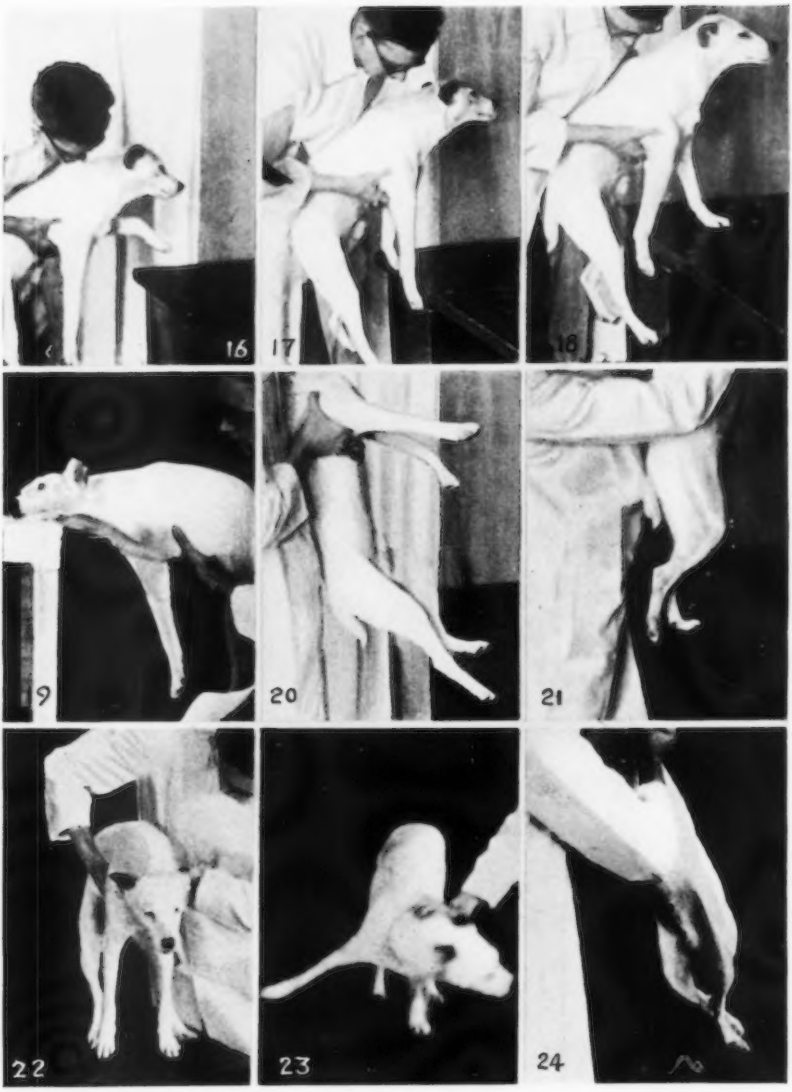
To illustrate paper by Clinton N. Woolsey.

PLATE XIII.



To illustrate paper by Clinton N. Woolsey.

PLATE XIV.



To illustrate paper by Clinton N. Woolsey.

PLATE XII.

FIG. 2.—Dog 30, photographed two months after removal of the left excitable cortex, showing extensor rigidity of the contralateral limbs and flexion of the ipsilateral ones while suspended in a hammock.

FIG. 3.—Same, from in front. Note fanning of toes of extended limbs.

FIG. 4.—Same animal, held back-to-examiner.

FIG. 5.—Dog 26, photographed two weeks after removal of the left excitable cortex, showing contralateral extensor rigidity.

FIG. 6.—Dog 10, from which the left gyrus proreus and left orbital gyrus were removed first without effect, photographed four months after a second operation at which the right sigmoid gyrus and gyrus proreus were ablated. Typical extension is seen in the limbs contralateral to the sigmoid lesion.

FIG. 7.—Dog 30, showing increased resistance to pressure on the sole.

FIG. 8.—Dog 30, illustrating the manner in which the ipsilateral limbs are used normally to escape from the hammock, while the contralateral limbs remain extended and exhibit deficient placing reactions.

PLATE XIII.

FIGS. 9 and 10.—Dog 26, photographed two weeks after removal of the left excitable area. When the side contralateral to the lesion is uppermost there is an accentuation of the normal upward concavity of the body. When the contralateral side is down the concavity is downward. The trunk musculature of the contralateral side is hypertonic and resists passive straightening of the body axis.

FIG. 11.—Dog 20, from which the left sigmoid gyrus was removed. There is extensor rigidity of the right limbs. The neck and shoulders are acutely flexed to the contralateral side by the hypertonic musculature.

FIG. 12.—Same animal, lying quietly on its back, showing extensor rigidity of the contralateral fore-leg.

FIG. 13.—Dog 30, illustrating the difference in readiness of the limbs to extend when pressure is applied above the elbow. Both have just become extended. The contralateral limb traversed the lesser angle. The difference is often much more marked.

FIG. 14.—Dog 30, made to walk backwards on the fore-legs. The ipsilateral limb executes stepping movements; the contralataral (right) one drags.

FIG. 15.—Dog 30, on its back, illustrating crossed extension reflex. This animal did not show extensor rigidity spontaneously in this position.

PLATE XIV.

FIG. 16.—Dog 30, illustrating the visual placing reaction of the fore-leg. The contralateral limb fails to place, remaining rigidly extended.

FIG. 17.—Same animal. The backs of both fore paws were simultaneously touched to the table edge. The ipsilateral foot is being lifted; the contralateral one does not react.

FIG. 18.—The ipsilateral foot has been placed upon the table. The contralateral leg has been over-extended by pressure against the table edge. At this point the right foot was raised and placed upon the table also.

FIG. 19.—Both fore-legs were held down while the chin was brought into contact with the underlying surface. Upon release of both limbs only the ipsilateral one was placed beside the jaw.

FIGS. 20 and 21 show for the hind-legs what figs. 17 and 18 do for the fore-legs.

FIG. 22.—When the animal was lifted off the table the contralateral feet left first. The difference was usually more marked.

FIG. 23.—The animal was pushed toward the contralateral side. Instead of effectively correcting for the displacement or maintaining its footing the left leg slipped from under the animal.

FIG. 24.—The contralateral hind-limb failed to correct its position when the body was moved lateralward. The ipsilateral foot, however, has stepped in the direction of the displacement.

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THE ENCEPHALIC CONTROL OF TONE IN THE MUSCULATURE OF THE URINARY BLADDER.

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Introduction.

After injuries to the spinal cord of man producing severe involvement of normal, voluntary micturition, the bladder, although it may contract automatically, never empties completely and there constantly remains residual urine. This was particularly well demonstrated by Head and Riddoch (1917) in their study of soldiers with complete transection of the thoracic portion of the spinal cord. Barrington (1925), on the basis of experiments with cats, localized in the cephalic portion of the hind-brain a centre controlling contraction of the bladder musculature. Following bilateral injury of small areas with the Horsley-Clarke stereotaxic apparatus, the contraction of the bladder musculature became faulty. These areas extended longitudinally from the level of the anterior end of the hind-brain in front to the middle of the motor nucleus of the fifth nerve below. The afferent impulses responsible for this motor control, according to Barrington, run principally with the parasympathetic fibres.

It is the current tendency in neurology to avoid the concept of isolated centres in the brain having specific functions, and to think of portions of the nervous system as large units correlating activity. On the basis of centres, it is difficult to understand an area controlling contraction of the bladder as removed from the cord and placed in the brain-stem. Taking a broader view-point, on the other hand, the brain-stem is known to have a powerful influence over the tone of the striated musculature of the body. It seems possible that a similar mechanism controls the tone of the smooth muscle in the bladder and that injury of this tonic mechanism or its pathway in the spinal cord may be responsible for the inability to empty the bladder completely. The present report deals with experiments which clarify this problem.

Methods.

Thirty-three adult female cats were used in the experiments. A fine glass cannula was inserted into the bladder through the urethra

and the free end attached by a three-way tube to a water manometer with a three-millimetre bore. Through the three-way tube fluid could be introduced into the bladder from a burette graduated to $\frac{1}{10}$ c.c. Water, warmed to body temperature, was allowed to flow into the bladder slowly at the rate of about 1 c.c. a minute. Readings were taken after adding each 5 c.c.

The glass catheter was not tied into the bladder but was held in place by the tone of the urethra and the sphincters. When micturition began, the catheter became loose in the urethra and fluid escaped around the catheter. If the reflex of micturition was damaged so that retention resulted, fluid escaped when the pressure in the bladder rose to a level sufficient to force the sphincter. The insertion of the catheter without tying made it certain that the bladder never became overdistended. The apparatus recorded the phenomena of tone, and contraction of the bladder-wall, and relaxation of the sphincters was demonstrated only as a part of the reflex of micturition.

The type of anæsthesia to be used in the experiments was the subject of considerable study. Barrington felt that the bladder did not empty completely under ether anæsthesia. In our experiments with the cats quiet under light ether anæsthesia, the bladder usually emptied normally and completely. The pressure readings were often abnormally high after the administration of ether. The chief objection to this method was that the ether was discontinued after decerebration, inasmuch as the animals no longer felt pain, and it seemed hazardous to compare the results of reflex contractions under ether with those obtained after the anæsthesia was discontinued.

Several experiments were then performed using as an anæsthetic dial ciba in urethane which acted constantly throughout the whole period of the observations. This was kindly furnished by the Ciba Company. In order to avoid any possible local effect upon the bladder, it was not injected intraperitoneally but intramuscularly in amounts of $\frac{1}{2}$ c.c. per kilogram. At least two hours were allowed to elapse between the administration of the drug and the beginning of the experiment. At the end of this time the preparation was extremely relaxed. A small amount of ether in addition was usually required at the beginning of the cerebral operation. Apart from this the anæsthesia was constant, so that the results of study of the bladder before and after decerebration are directly comparable.

The results of the experiments with these two anæsthetics agree in all important details. The bladder emptied reflexly upon a constantly

smaller volume of fluid with dial than with ether. Certain facts were more clearly brought out with the use of ether. It is necessary to report in detail two typical experiments, one performed with the use of dial ciba and the other with ether.

Experimental Findings.

(1) *Experiment utilizing Dial Ciba in Urethane as the Anæsthetic.*

(a) Reflex micturition in the intact animal.

After the cannula was inserted in the bladder of the cat, it was necessary to adjust the apparatus in such a way that the opening on the lateral side of the end of the catheter lay free in the bladder and accurate pressure readings were obtained. This was the most difficult part of the technical procedure. It is well known that the pressure in the bladder never falls to zero even when the viscus is entirely empty, and the pressure in the empty bladder in our experiments varied from 3 to 5 cm. of water. The initial reading was considered to be accurate when it lay within this range and when the column of fluid showed respiratory oscillations. This indicated that there was no block interfering with the readings.

Fluid was then slowly injected into the bladder, and the changes of pressure in the manometer were watched continuously and recorded after each 5 c.c. of fluid had entered. A graph showing the changes in pressure in the intact preparation is given (fig. 1 A) with the equal increments of volume plotted on the ordinates and the increments of pressure change on the abscissæ. In this case the initial pressure in the empty bladder was 4·5 cm. of water. With the addition of the first 5 c.c. of fluid the intravesical pressure rose to 13·2 cm. and remained below a pressure of 15 cm. of water until over 80 c.c. of fluid had been injected. The pressure then rose rapidly and complete evacuation of the bladder occurred when 94·2 c.c. had entered the viscus. As the volume of fluid was increased, waves representing weak contractions of the bladder musculature became superimposed upon the respiratory rises and caused variations, often of several centimetres, in the upper and lower readings. The lowest readings for a given period were always recorded for the sake of uniformity. When micturition occurred, the fluid expelled was collected, measured and compared with the amount introduced, giving a check of the ability of the bladder to expel the total contents.

This graph, showing variations of pressure in the cat's bladder with the addition of equal increments of volume, clearly illustrates the well-known fact that this hollow viscus can accommodate greatly increased amounts of fluid without altering materially the pressure within its walls.

Although the volume initiating reflex micturition varied for different preparations, it was remarkably constant for a given individual. To

determine this readings were made upon a single cat on different days and with the use of each of the two anæsthetics, ether and dial ciba. The pressure readings were raised slightly by the administration of ether, and the bladder emptied with a somewhat smaller volume under dial. The volume of fluid necessary to induce reflex micturition was commonly around 60 c.c., although it could be lower and was commonly much higher.

The most convincing experimental results were obtained from individuals that showed reflex micturition only after more than 100 c.c. of fluid had entered the bladder. In these cases it was possible to

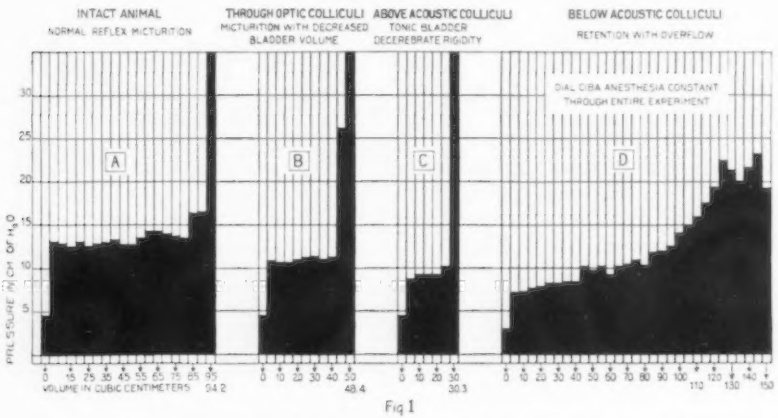

FIG. 1.—The addition of equal increments of fluid to the bladder volume is plotted on the ordinates, and the intravesical pressures in centimetres of water on the abscissæ. Dial ciba gave a constant anæsthetic for these results recorded from a study of a single preparation. Further description of the experiments is given in the text.

show the change in volume initiating micturition after decerebration. The volume at which the bladder emptied in a given cat was always checked at least twice before the experiment was continued; it was necessary that the results should agree within 5 c.c. Many cats were rejected after initial readings on the normal bladder because the pressure readings were very high or because the viscus did not empty normally. These difficulties were ascribed largely to the anæsthetic, but there is undoubtedly great individual variation in bladder pressure and the volume required to produce reflex relaxation of the sphincters. The pressure readings were always somewhat high inasmuch as they were recorded simultaneously with the slow flow of fluid into the bladder under pressure.

(b) The effect upon micturition of removal of the fore-brain to mid-thalamic level.

The surface of the fore-brain was exposed bilaterally after the carotids had been tied, and a transverse cut was made through the nervous system above the mid-brain and through the mid-thalamic region. After this section there was no increased tonus in the extremities. When the reflex of micturition was studied, it was found that the bladder emptied on a volume 18 c.c. smaller than in the intact preparation. This result is not plotted in the graph. The significance of this variation, small in this particular experiment, will be discussed later in connection with other records made under ether anæsthesia.

(c) The effect upon micturition of transection through the optic colliculi.

The second transverse section through the brain-stem passed through the cephalic portion of the optic colliculi. There was no appreciable increase in tone in the striated musculature of the extremities following this incision. The results in reference to the bladder are shown on fig. 1 B. The initial reading with the bladder empty was similar to that in the intact preparation, 4·5 cm. After the introduction of fluid the intra-vesical pressure remained lower than in the intact cat, and stayed constantly below 11·5 cm. of water instead of rising as high as 14·5 cm. of pressure. When the volume of fluid in the bladder had reached 40 c.c. the pressure rose very rapidly and forcefully and the bladder emptied on a volume of 48·4 c.c. of water. The most significant finding is the fact that the bladder, which in the intact animal had emptied only when it contained 94·2 c.c., now emptied on 48·4 c.c. of water. There were other changes. In the intact animal the musculature of the bladder showed rhythmical waves of contraction that increased in strength as the viscus became full; after removal of the fore-brain these waves of contraction were much less conspicuous. Moreover, the contraction of the musculature after the reflex of micturition was initiated was much more precipitous and stronger after transection of the brain-stem than it was before.

(d) The effect upon micturition of transection above the acoustic colliculi.

After the preceding findings had been confirmed, the brain-stem was cut through at a slightly lower level, through the cephalic edge of the acoustic colliculi. Immediately after this cut, marked extensor tone could be demonstrated in the extremities. The volume of fluid in the bladder that was required for reflex micturition was then determined (fig. 1 C). The initial reading with the bladder empty was 4·5 cm., as in the intact animal. When

further fluid was introduced the pressure remained below 10 cm. of water until the bladder emptied. This reading was not only lower than for the unoperated cat, but also lower than after transection through the optic colliculi. After 30 c.c. of water had been introduced, the bladder contracted forcefully and quickly and the viscus emptied completely. No significant rise in pressure occurred before the force of the contraction became great enough to empty the bladder.

After section through the cephalic edge of the acoustic colliculi, the bladder was found to empty reflexly and completely on less than a third of the amount of fluid required before the operation, and on considerably less than after transection through the upper edge of the optic colliculi. When the empty bladder was palpated through the abdominal wall it was felt to be very tightly contracted.

Data were obtained suggesting that the relaxation of the sphincters was more complete after transection of the brain-stem at this level than in the normal cat under the anæsthetic. In certain of the preparations before the operation, the relaxation of the sphincters with reflex micturition was very incomplete, and this was attributed to the anæsthetic. After decerebration with the same anæsthesia still operative, the relaxation of the sphincter was much more perfect.

(*c*) *The effect upon micturition of transection of the brain-stem below the acoustic colliculi.*

The fourth section was made well below the acoustic colliculi; the increased tone in the extremities was not invariably lost and the cat breathed normally (fig. 1D). Now the picture of bladder activity was quite changed. The initial pressure with the bladder empty was 3 cm. of water, and the pressure rose after the introduction of fluid but always remained below 12 cm. of water until 90 c.c. had been introduced, the amount that stimulated micturition in the intact animal. The pressure readings were somewhat lower than in the record before operation. On the introduction of further fluid into the bladder, the pressure rose in graded increments and continued to rise until 125 c.c. had been introduced. Although waves of bladder contraction occurred, there was no well-sustained contraction that increased the pressure markedly and led to evacuation of the viscus. After 125 c.c. had been injected, the pressure was recorded as 23·5 cm. At this point there was a relaxation of the sphincter and a small amount of fluid escaped. During the injection of the next 10 c.c. of fluid the pressure fell, but rose again and each time it reached 23·5 cm. a small amount of fluid escaped. This experiment could be continued almost indefinitely without the development of any adequate reflex micturition. The bladder now showed retention with overflow, and the sustained contraction of the musculature required to empty the viscus was lost.

(2) *Experiment utilizing Ether as the Anæsthetic.*

It is impossible at present to speak with certainty of the action of an anæsthetic upon the different portions of the nervous system, particularly its autonomic portion. The results obtained with the dial anæsthesia are reported to show that changes in the capacity of the bladder essential for reflex micturition are obtained after section of the nervous system when the anæsthesia remains constant throughout the experiment. The results when using ether as an anæsthetic bring out the part played by the cerebral motor cortex in the normal control of tone in the bladder musculature. Repetition of these results led to the conclusion that they were significant, the more so inasmuch as the ether anæsthesia was maintained at the same level after portions of the cortex were removed and indeed until the preparations were decerebrated. With dial care was taken to produce a deep anæsthesia which is reflected in the results of the experiments.

(*a*) *Reflex micturition in the intact animal.*

The results of a typical experiment using ether as the anæsthetic are shown in fig. 2A; the graphs are made after the same method used in the first table. The initial pressure reading from the intact preparation with the bladder empty was 5 cm. of water; with the introduction of the first 5 c.c. of fluid the pressure rose to 10·2 cm. and remained below 15 cm. until over 125 c.c. of water had been introduced into the bladder (fig. 2A). The pressure readings then rose fairly rapidly and after 155 c.c. had been introduced was over 30 cm. At this point the bladder emptied reflexly. The bladder of this cat had a large capacity.

(*b*) *The effect upon micturition of removal of the left motor cortex.*

After the normal capacity of the bladder had been ascertained, the left motor cortex was quickly exposed and cut away. The anæsthetic was con-

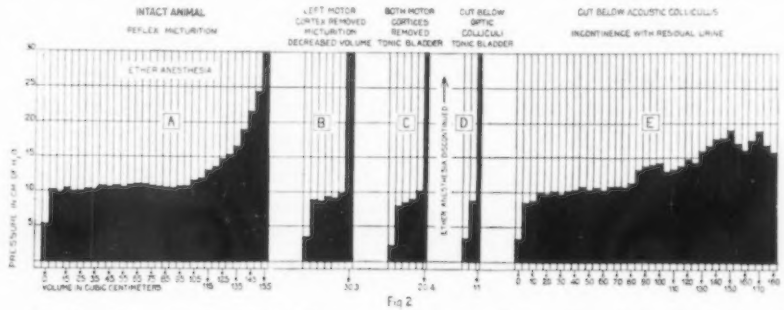

Fig 2

FIG. 2.—These results obtained from a single preparation under ether anæsthesia are plotted in the same manner as in fig. 1, and the results are further discussed in the text.

tinued and another determination of the capacity of the bladder was made (fig. 2B). The initial reading with the bladder empty was somewhat lower than before, 3·5 cm. as against 5 cm. The pressure rose with the introduction of water to 8·8 cm. and remained below 10 cm. of water until over 25 c.c. had been introduced into the viscus. The pressure then rose very rapidly to 33 cm. After 30·3 c.c. had entered the bladder, the sphincters relaxed, allowing the fluid to be expelled forcefully. Under the same degree of anæsthesia a bladder that in the intact animal showed an intravesical pressure of 30 cm. only after 155 c.c. of water had been introduced, now showed a pressure of 33 cm., as well as forceful contractions of the bladder musculature after 30·3 c.c. of water had entered the viscus.

(*c*) *The effect upon micturition of removal of both motor cortices.*

With the depth of the anæsthesia held constant the right motor cortex was in like manner exposed and removed and another record of bladder activity was made (fig. 2C). The pressure after an initial reading of 2·4 remained below 10 cm. of water until 20 c.c. of fluid had entered the viscus; then the pressure rose so suddenly and rapidly that the bladder emptied completely around the catheter on a capacity of 20·4 c.c. and at a pressure of 24 cm. of water. Removal of the second motor cortex was followed by a second decrease in the size of the bladder so that it emptied on 20·4 c.c. as opposed to 30·3 c.c. after the cortex had been ablated on one side. Moreover, a bladder which held 155 c.c. in the intact preparation now contracted on 20·4 c.c. The rise of pressure with each of these sections became increasingly sudden and forceful, and the expulsion of fluid from the urethra more complete.

(*d*) *The effect upon micturition of transection below the optic colliculi.*

The preparation was then decerebrated by transecting the brain-stem below the optic colliculi; following this operation the ether was discontinued. No time was allowed to elapse to enable the cat to recover from the anæsthetic, but as soon as the bleeding was controlled and respirations were normal, the investigation of the bladder was continued (fig. 2D). The animal showed increased extensor tone of the extremities. The initial pressure with the bladder empty was 3·2 cm. and rose after 5 c.c. of water had been introduced into the viscus to 8·2 cm. When 11 c.c. of water had entered the bladder the pressure rose quickly to 24 cm. and the bladder emptied completely around the catheter.

After transection below the optic colliculi, the bladder emptied reflexly on 11 c.c. of water instead of on 155 c.c. as in the intact animal and 20·4 c.c. after removal of both motor cortices. The expulsion of fluid was forceful and the pressure rose suddenly without initial oscillations.

(e) *The effect upon micturition of transection below the acoustic colliculi.*

After the brain-stem was transected below the acoustic colliculi, the readings obtained from the bladder were greatly changed (fig. 2E). The initial pressure was 3·4 and remained below 15 cm. until over 125 c.c. of water had entered the bladder. Then the pressure readings rose very slowly: after 155 c.c. of fluid had entered the viscus and the pressure was 19·2 c.c. the sphincter relaxed and a small amount of water escaped from the urethra. The contraction of the muscle was very weak and after a small amount had escaped the sphincter tightened again and the pressure fell to 17 cm. The bladder now showed retention with overflow so that some fluid always escaped when the pressure rose to 19 cm., but the bladder never emptied. The transection of the brain-stem was below the centre controlling the tone and contraction of the bladder musculature.

Discussion.

These experiments confirm the findings of Barrington that the stimuli responsible for prolonged contraction of the musculature of the bladder essential for normal micturition are mediated from the region of the upper end of the hind-brain. Indeed, our work confirms exactly his findings concerning the level in the brain-stem of this control. It is not necessary, on the other hand, to postulate a unique and isolated centre for the control of the muscles of the bladder at this level, but rather to realize that tone in the bladder is determined by similar reflex pathways to those controlling tone in the striated muscles of the extremities. The technique used in the present experiments gives a more or less quantitative method for measurement of increased tone, whereas no good quantitative standard can be applied to the problem of tone in striated muscles.

The experiments with ether show convincingly that the tonic centre is normally controlled by both cerebral hemispheres. After the motor cortex has been removed on one side the bladder accommodates to a smaller volume of fluid before reflex micturition is initiated, and after both motor cortices have been removed the volume required to induce the reflex is further reduced. There are probably other controlling mechanisms in the fore-brain, either subcortical or in other portions of the cortex, for another reduction in volume is obtained after transections below the optic colliculi. The exact nature of this control has not been determined. If the transection of the brain-stem is then made below the acoustic colliculi, reflex micturition is abolished and the bladder shows retention with overflow. The tonic reflex responsible for contractions of the

musculature adequate to empty the viscus have been abolished. We believe, therefore, that there is in the upper portion of the hind-brain a mechanism controlling tone in the smooth musculature of the bladder similar to the reflexes localized in the same region which control tone in the striated muscles of the extremities. This conclusion is unique in that a mechanism of this type has never been postulated for smooth muscle. The tonic reflex is responsible for prolonged and forceful contraction of the musculature necessary completely to expel the urine. The operation of this reflex is normally controlled and held in check by areas in the fore-brain and particularly from the cerebral motor cortex. When these inhibitory and governing mechanisms have been removed the tonic reflex overacts, as in the present experiments. After the connections of this tonic reflex arc with the spinal cord have been impaired in any way, incontinence with overflow is the immediate result and residual urine is always present even if automatic micturition becomes established.

That the tonic reflex for the bladder musculature is not the same as that controlling tone in the extremities is quite clear. Barrington could place lesions injuring bilateral areas in the medulla producing incontinence with overflow, but these preparations showed almost no disturbances of tone in the extremities. Using dial anæsthesia, the tonic reflex in the hind-brain could be released without producing decerebrate rigidity and, conversely, after a section below the acoustic colliculi the tonic bladder reflex was lost, but decerebrate rigidity still persisted.

These experimental findings serve to explain certain clinical symptoms. Patients with neurological lesions of the brain and spinal cord often complain that they have to micturate very frequently and that it is extremely difficult to hold back the urine after the first sensory impulses indicating distension of the bladder are received. The latter symptom is called imperative micturition. It indicates that the bladder can no longer be voluntarily relaxed to hold more fluid, and also that the contractions of the bladder musculature are immediately very forceful. It is probable in these cases that there has been a lesion of the inhibitory mechanism which governs the tonic mechanism in the hind-brain, and the condition is similar to that produced in the experiments by removal of one or both motor cortices or transection through the optic colliculi. The bladder empties upon small quantities of fluid and the contractions of the musculature are sudden and forceful.

Cases reported in the literature show that these abnormalities may be produced by bilateral lesions of the motor cortex. Thus Holmes and

Sargent (1915) reported cases of thrombosis of the superior longitudinal sinus. One patient explained that he was incontinent because he "could not hold his water for over five minutes." Imperative micturition also occurs when the lesion seems to be localized entirely in the spinal cord. This, of course, suggests that the inhibition of tonus is effected not at the level of the tonic reflex in the brain-stem, but through the motor cells of the spinal cord. Finally, it has already been explained that injury of the tonic reflex arc has a profound effect upon micturition in man.

The question may be raised as to the part played by contraction of the abdominal muscles in these experiments. Barrington rendered the abdominal wall functionless with curare and found that this had no effect upon his results. Although abdominal contraction may have a part in reinforcing micturition, it is by no means essential for the normal functioning of this reflex. The abdominal wall can be left open for only short periods of time without impairing the function of the musculature. However, we have opened the abdomen while the reflex was active without any impairment of its function.

One of the authors (Langworthy and Richter, 1930) has previously shown, using the galvanic skin response as a criterion of sweat-gland stimulation, that sweating, a function controlled by the sympathetic portion of the autonomic nervous system, was produced by stimulation of areas in the cerebral motor cortex and of all the well-known motor pathways extending from the brain to the spinal cord. The conclusion was reached that the activity of the preganglionic sympathetic cells is controlled by the same tracts that influence the somatic motor cells of the spinal cord. The present experiments suggest that tone in the bladder musculature is controlled by reflex pathways similar to those controlling tone in striated muscles. This discussion of the reflex of micturition probably has to do almost exclusively with the control of the parasympathetic reflex arc by the brain rather than the sympathetic portion of the autonomic nervous system as in the case of sweat-gland stimulation.

Summary.

The normal act of micturition is dependent upon a well-sustained contraction of the smooth musculature of the wall of the bladder. With lesions of the nervous system below the mid-brain affecting micturition, this contraction is faulty. The experiments were performed upon cats, using as anæsthetics dial ciba, which acts uniformly throughout the

experiment, or ether. After decerebration through the optic colliculi the bladder emptied completely on as little as one-fourteenth the volume of fluid required to produce reflex micturition in the intact, anæsthetized preparation. Under these conditions the pressure rose very rapidly and the contraction of the muscles was forceful. Transection of the brain-stem below the acoustic colliculi abolished this reflex and no contraction sufficient to empty the bladder occurred. The bladder then showed retention with overflow. The conclusion was reached that tone in the musculature of the bladder is controlled by similar mechanisms to those that control tone in the striated musculature. There is evidence that the control of this tonic mechanism is largely a function of the cerebral motor cortex and is effective at the level of the spinal cord. The tonic control is carried out from areas in the cephalic portion of the hind-brain. A study of bladder abnormalities in man serve to illustrate the experimental findings.

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OBSERVATIONS ON THE PARALYSED BLADDER.

BY GORDON HOLMES.

THE observations recorded in this article were made in base hospitals in France during the War, mainly in the winters of 1915 and 1916. They have not been previously reported for various reasons, mainly because it was hoped to complete the investigation at the termination of the War by the examination of the later stages of paralysis of the bladder. This was undertaken in a few cases and the results obtained will be referred to. It was also realized that the methods employed were not adequate to solve many of the problems which arose, especially during the stages of recovery of tone in the musculature of the bladder. As more satisfactory methods of investigation have been devised by Denny-Brown and Graeme Robertson [1] these observations are now published as they throw some light on the condition of the bladder in the recent and acute phases of its paralysis as a result of spinal lesions, in which stage the opportunity of examining it is not so frequently met in civil practice.

Material.—With a few exceptions these investigations were made in men who had, as far as could be judged by clinical signs supplemented by radiological and surgical observations, complete transverse lesions of the spinal cord due to gunshot wounds. In a few cases with injuries of the sacral segments or of the cauda equina the lesions may have been incomplete. More than thirty cases in all were examined, and the injuries in these involved all regions of the cord from the highest cervical segments to the cauda equina.

In several cases the first examination was possible within two days of the infliction of the wound, but owing to the exigencies of hospital service during the War few could be kept under observation for long periods. Most men who received spinal injuries were evacuated to England within a week or ten days, but it was fortunately possible to retain a few cases for several weeks during periods in which there were few casualties. In some of these repeated examinations were made.

Method of examination.—The bladder was first emptied under strict aseptic precautions and a note was made of the amount of urine it

contained. As it was found that the observations might be influenced by the degree of distention of the bladder before the examination, it was in most of the cases emptied half to one hour before measurements were made. A sterile saline solution was then introduced through the catheter at a slow and uniform rate and under pressure only just sufficient to allow it to enter freely. After each unit of volume, which was usually either two or four fluid ounces (60 or 120 c.c.), had entered the pressure within the bladder was recorded, and successive observations were made until the vesical pressure had reached a considerable height, or until the bladder contained an amount of fluid beyond which it was not considered advisable to go. The measurement of intravesical pressure was therefore intermittent, but the records were made at short intervals and any significant variations of pressure between the measurements were noted by an assistant.

In other experiments the changes of pressure within the bladder, when it contained a constant volume of fluid, were recorded. These observations were usually continued for several minutes, sometimes for as long as half an hour.

The apparatus used was necessarily simple. A large catheter was passed and held in position by an assistant. From it a rubber tube of equal calibre led to a large cylindrical reservoir containing sterile fluid which could be moved up and down along a scale marked in centimetres which indicated the height above the symphysis pubis, the point from which it was found most convenient to measure the head of the fluid. In order to obtain measurements of pressure the reservoir was raised or lowered till the level of fluid within it remained constant at a mark on its side. The height of this level was then read off on the scale and recorded.

A catheter and a tube of large bore were necessary to allow the fluid to escape freely from the bladder to the reservoir or to enter the bladder when the pressure within the latter varied rapidly, or when the reservoir was raised or lowered to determine the intravesical pressure. On the other hand, in order to introduce fluid slowly a tube of small lumen was essential. A by-pass was therefore provided in which a glass pipette of small calibre was inserted. During introduction of fluid into the bladder the main tube was compressed so that the fluid entered through the narrow by-pass only, but while the intravesical pressure was being recorded both the main tube and the bye-pass remained open.

After each examination the measurements were plotted on squared

paper : the amount of fluid which the bladder contained on the abscissa, the corresponding pressure within the bladder on the ordinate. A curve of the volume-pressure relations was in this way obtained. The same scale has been used in all the tracings reproduced here.

This method of examination proved to be satisfactory in dealing with inert bladders in the early stages of paralysis, but in the normal, and in bladders regaining tone and reflex activity, rapid changes of pressure often occurred which could not be accurately measured. These can be demonstrated only by a method which records volume and

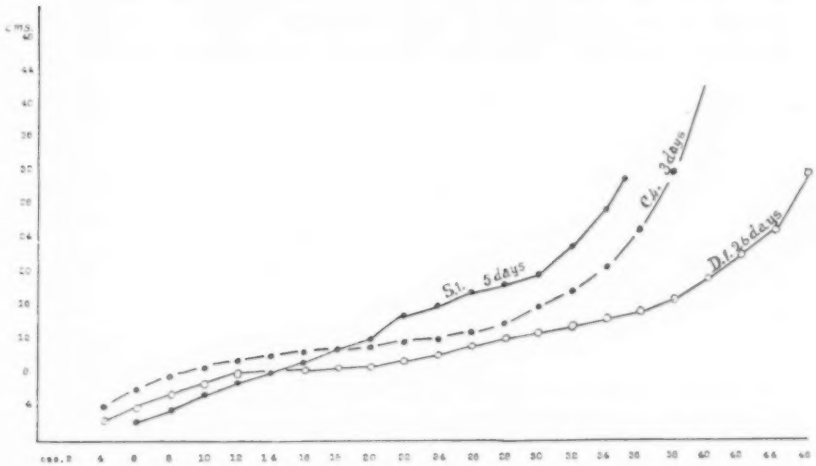

FIG. 1.—Tracings showing the volume-pressure relations obtained on filling slowly three different bladders. The lesions involved the first dorsal, fourth cervical and first sacral segments. The level of the lesion and the number of days after the infliction of the wound are shown on each tracing.

pressure continuously, but such results as I obtained throw some light on the nature of early vesical paralysis and its recovery.

For the sake of simplicity the state of the bladder paralysed by a complete lesion of the cord will be described in the three successive phases through which it passes, but it must be understood that there is no rigid separation between these phases, which represent only stages in gradually progressing recovery of tone and activity.

First phase.—When the bladder of a man with a recent transverse lesion of the spinal cord was filled slowly, usually no pressure could be recorded, that is, the level at which the fluid in the reservoir remained stationary was below the level of the pubis as the patient lay on his

back, until 4 to 8 oz. (120-240 cm.) of fluid was introduced. The amount of fluid that gave the first measurable pressure varied within narrow limits; as a rule it was greater when the bladder had been distended immediately before the examination, but in most of my cases it had been emptied half to one hour before the experiment.

As fluid was introduced the intravesical pressure rose slowly and gradually, never interrupted by an increase or fall unless some extraneous factor, as coughing, straining or pressure on the abdomen, came into action. The tracing obtained when the pressures were plotted was at first almost flat (fig. 1). No striking rise occurred until the pressure reached about 12 to 20 cm. of water, or till 20 to 30 oz. of fluid had entered the bladder. Then the curve rose more rapidly and when the

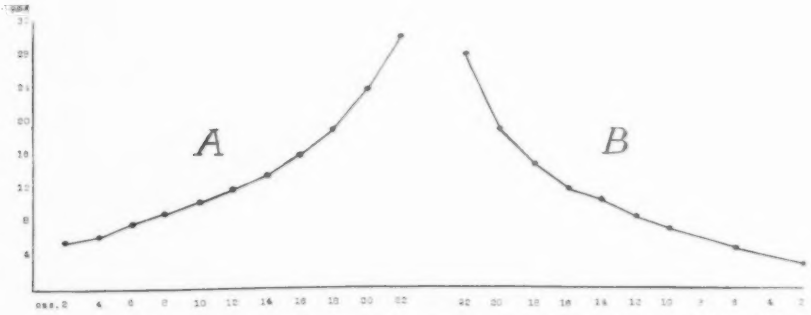

FIG. 2.—Lesion of fifth lumbar segment. Experiment 17 days after infliction of the wound. A, curve obtained on filling the bladder slowly; and B, that on emptying it at the same rate.

pressure reached about 40 cm., no more fluid could be introduced under pressures which were considered safe; the bladder had apparently reached the limit of its distensibility. Even then no signs were observed of an attempt of the bladder to empty itself.

If the bladder was now emptied slowly and the pressure was recorded after each unit of volume was removed the intravesical pressure fell gradually, and when the successive measurements of volume and pressure were plotted they reproduced a tracing practically the reverse of that obtained on slowly filling the bladder (fig. 2).

The recently paralysed bladder therefore presented the properties of elasticity only; that is, it resumed its original size or volume when the distending force which expanded it ceased to act, and in returning to its contracted volume the pressures which its walls exerted on its

contents were equivalent to the force which expanded it to each similar degree.

When an amount of fluid sufficient to produce a measurable pressure in the bladder was kept constant and the pressure was recorded at short intervals no significant variations in the pressure, apart from those associated with respiration, were observed for several days or even three or four weeks after the infliction of the wound. When plotted the measurements of pressure formed practically horizontal lines (fig. 3). If the intravesical pressure were raised suddenly by pressure on the abdomen, coughing, or a deep breath, it fell at once again to its original level.

Within the first ten days or so after the onset of the paralysis the

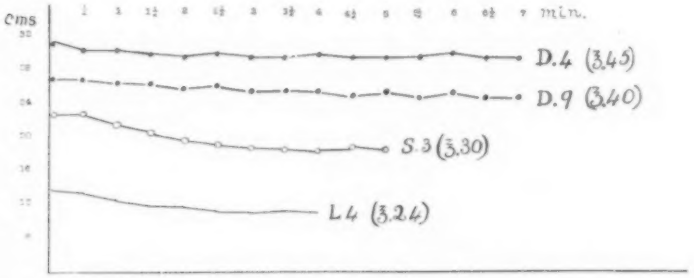

FIG. 3.—Tracings obtained in four cases by measuring the intravesical pressures at half-minute intervals when the volumes of fluid within the bladder were constant. The level of the lesion and the number of ounces of fluid in the bladder are shown to the right of each tracing.

tracings obtained from these methods of investigation were practically identical in all cases examined. When the bladder had been greatly distended before the records were made, or if the state of the patient was unsatisfactory owing to sepsis of the wound or other complications, the curves were generally flatter, that is, intravesical pressure rose more slowly on the introduction of fluid, in other words the elasticity of the vesical musculature was diminished. On the other hand the occurrence of cystitis—and it was rarely possible to keep bladders which required frequent catheterization aseptic—had during this stage apparently little influence.

From these series of observations it is obvious that the recently-paralysed bladder behaves as an inert elastic bag, and that it shows no tendency to adapt itself to its contents, or to react to the tension to which its walls are exposed.

The condition just described was always found when the bladder was paralysed by a transverse lesion at any level of the cord or of the cauda equina, in fact in the long series of patients examined no difference could be recognized, in the early stages of the injury at least, between cases in which the spinal origin of the hypogastric nerves had been destroyed or the cord had been injured above it, and those in which it escaped owing to the lesion lying below the 12th thoracic segment. Further, the effects on the bladder were very similar whether the lesion lay in the upper segments of the cord, or destroyed the sacral

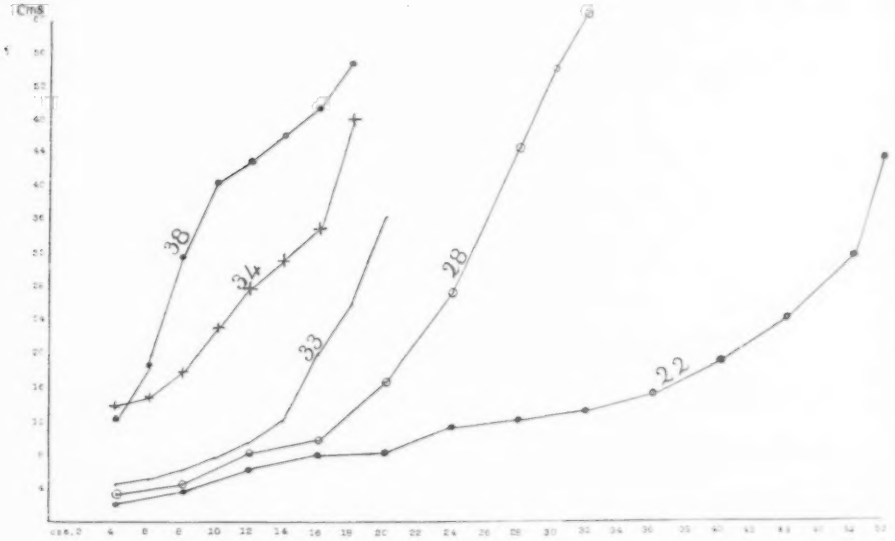

FIG. 4.—Five records showing the volume-pressure relations when the bladder was filled slowly on the 22nd, 28th, 33rd, 34th and 38th days after the onset of a complete transverse lesion of the first dorsal segment of the cord.

segments or their roots in the cauda equina. In both cases there was for a time apparently complete abolition of the nervous control of the bladder, which functioned only as an elastic bag.

From these observations the conclusion seems inevitable that a transverse lesion of any segment of the cord produces a state of severe depression, or even abolition of function, i.e., spinal shock, in the vesical mechanisms in the isolated portion below the level of the injury.

Second phase.—When repeated examinations were made on successive days or at frequent intervals no change could be as a rule observed till two or three weeks after the onset of the paralysis.

As a rule the first change was an increasing resistance to the introduction of fluid; for instance, eight or even more ounces of fluid may have been hitherto necessary to produce a measurable pressure, but now a smaller amount might raise intravesical pressure to 10 or 12 cm. of water. The pressure curves also rose more rapidly (fig. 4). The amount of fluid which could be introduced into the bladder was also considerably less than hitherto. Frequently, too, the curve obtained from plotting successive measurements was less regular, particularly if any interruption or delay occurred during the experiment.

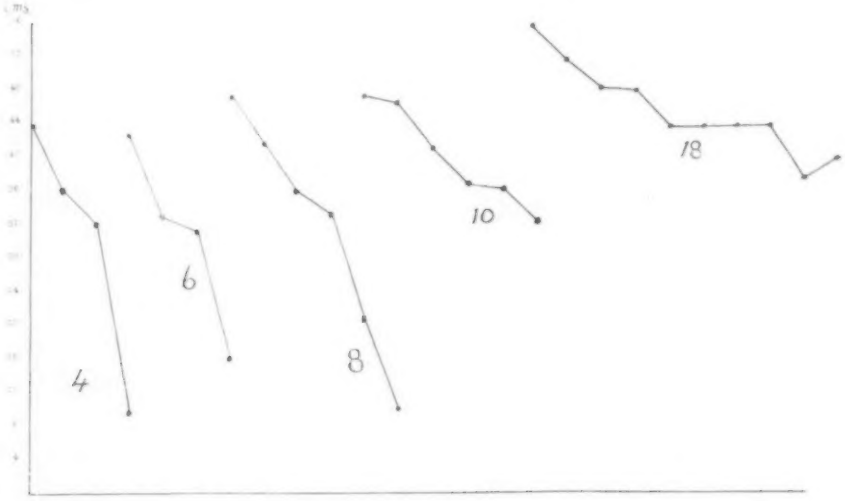

FIG. 5.—A series of tracings showing the fall of intravesical pressure after 4, 6, 8, 10 and 18 oz. of fluid had been in succession introduced into the bladder. In each instance the pressures were recorded at half-minute intervals.

If, when the intravesical pressure had been raised to a certain level the volume of fluid was kept constant, the pressure quickly fell, at first rather rapidly and then more slowly. This occurred no matter what the original pressure was, but the fall was usually greater and more rapid when the bladder contained a small amount of fluid only (fig. 5). When, however, a certain level of pressure was reached this level remained unchanged, apart from slight oscillations associated with respiration, for considerable periods, at least up to several minutes.

The pressure curves obtained during evacuation of the bladder were also now less regular; frequently the removal of a small amount of fluid

led immediately to a considerable fall of pressure, which might rise again slightly before becoming steady.

At this stage the bladder had to some extent acquired again the property of adapting its size to its contents; its muscular wall had evidently regained some tone. The muscles of the paralysed limbs were at this time still quite toneless, and the reflexes of the legs were usually absent.

It is worthy of note that these manifestations of tone appeared even when the sacral segments of the cord or the cauda equina were injured, but within the first few weeks of the infliction of the wound it was more difficult to determine the severity of the lesion when the roots were involved than when the cord was wounded. In the case from which

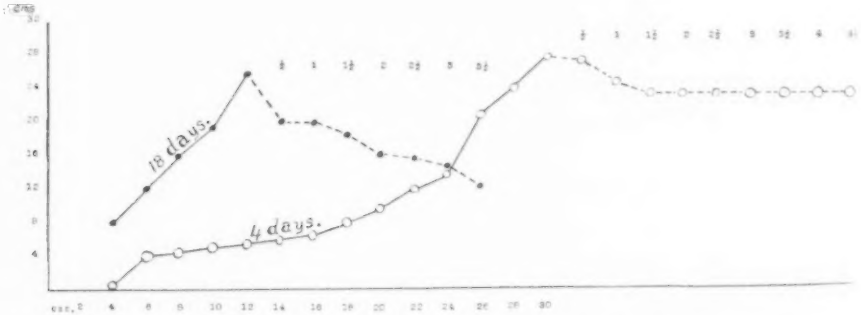

FIG. 6.—Two tracings showing the filling curves and the changes in pressure to constant volumes of fluid, 4 and 18 days after severe injury to all the sacral roots in the cauda equina. Time is recorded above in half minutes.

the readings in fig. 6 were obtained the clinical symptoms indicated a severe lesion of all the sacral roots; there was evidently a considerable return of tone on the eighteenth day as compared with the fourth day after infliction of the wound. This recovery of tone can be seen in another case (fig. 7) in which the cauda equina was injured by a large piece of metal which entered the vertebral canal through the fourth lumbar lamina and produced complete loss of sensation on all the sacral root areas on both sides and on the fifth lumbar area also on the left. There was no recovery of sensation during the three weeks the patient remained under observation.

Third phase.—The stage of simple tonicity of the bladder was generally of short duration and passed gradually into the third phase, the distinguishing feature of which was the occurrence of sudden con-

tractions of the bladder producing increases of intravesical pressure, or even the escape of fluid or extrusion of the catheter.

The tone of the musculature was evidently still increasing, for the curves obtained by plotting the initial pressures against the volumes which the bladder contained were steeper than hitherto (fig. 4, thirty-four and thirty-eight days). Less fluid could be introduced under moderate pressure, and the bladder adjusted itself more readily to its content; consequently the intravesical pressure no longer bore any definite relation to the volume of fluid within the bladder.

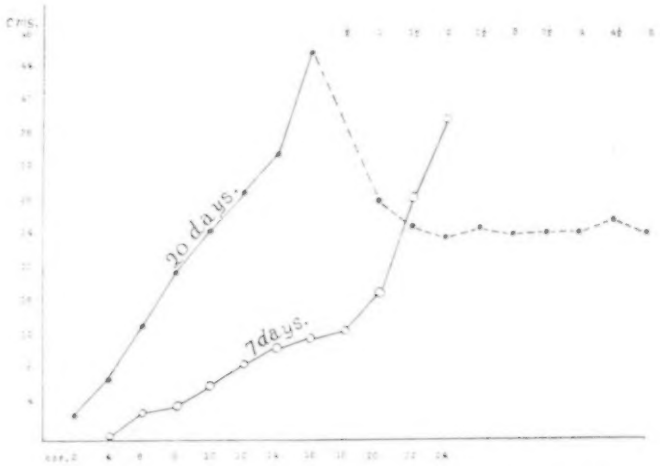

FIG. 7.—Two filling curves obtained 7 and 20 days after the onset of a lesion of the cauda equina. On the 20th day, after 16 oz. of fluid had been introduced, this volume was kept constant and the intravesical pressure was recorded at half-minute intervals for five minutes.

When the volume of fluid was kept constant the pressure frequently varied, rising and falling within wide ranges. These oscillations of pressure occurred irregularly and often were apparently spontaneous, at least they could not be associated with any other phenomenon.

They were generally not recognizable till the third or fourth week after the onset of the paralysis, and in some cases they appeared before the muscles of the legs had recovered tone or reflex spasms had developed. Two tracings representing these oscillations of pressure in one patient are reproduced. In one experiment (fig. 8), 10 oz. of fluid raised the intravesical pressure to 44 cm. of water, but it soon began to

fall, at first abruptly, then more slowly, so that after two minutes it was little more than half its original height. It remained at this level or with slight variations for about four minutes, when it rose so suddenly that some of the fluid was evacuated into the reservoir with such force as to indicate a powerful and abrupt contraction of the bladder. The pressure then subsided quickly to 28 cm., and later fell more gradually, so that nine minutes after the experiment began it was only 14 cm. Later, without obvious cause, another small rise occurred. Sometimes several such contractions of the bladder could be observed in succession

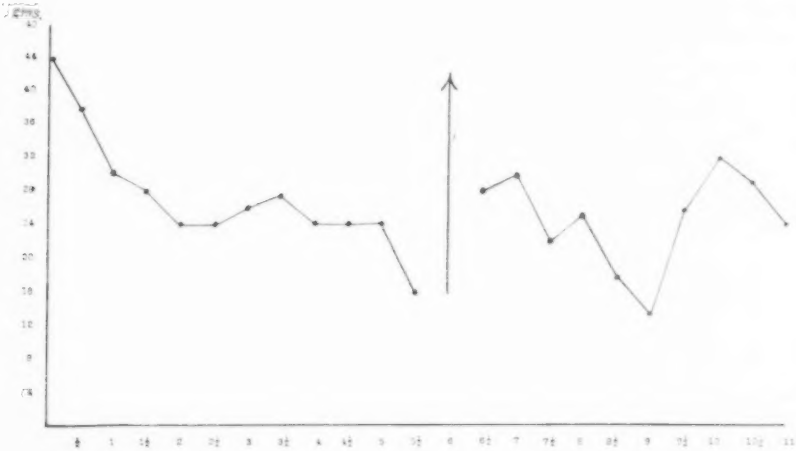

FIG. 8.—To show the variations in intravesical pressure when the bladder contained 10 oz. of fluid. The measurements of pressure were recorded at half-minute intervals. The arrow indicates a sudden rise of pressure and escape of some fluid into the reservoir. A transverse lesion of 1st dorsal segment 34 days after onset.

at fairly regular intervals (fig. 9), especially in the early stages of this phase.

The amount of fluid which the bladder contained had little influence on these contractions, but they were observed only when the intravesical pressure was at least moderately high. The experiments recorded in figs. 8 and 9 were made on successive days; on the thirty-fourth day 10 oz. of fluid raised the pressure to 44 cm., but on the following day 20 oz. produced a pressure of only 38 cm.

These oscillations of pressure were observed in bladders paralysed by lesions at different levels of the spinal cord, but they seemed to develop later and to be less pronounced when the lower segments were injured. I have no definite record of them occurring after complete

division of the cauda equina, as when these investigations were made there was no opportunity to keep patients with such lesions sufficiently long under observation, but slight variations in pressure were seen in cases in which the sacral roots had been injured three or four weeks previously.

Though these sudden contractions of the bladder often occurred apart from any other disturbances, they were sometimes associated with reflex spasms of the legs and abdominal muscles if the spinal lesion is sufficiently high for these to develop. They could also be excited by

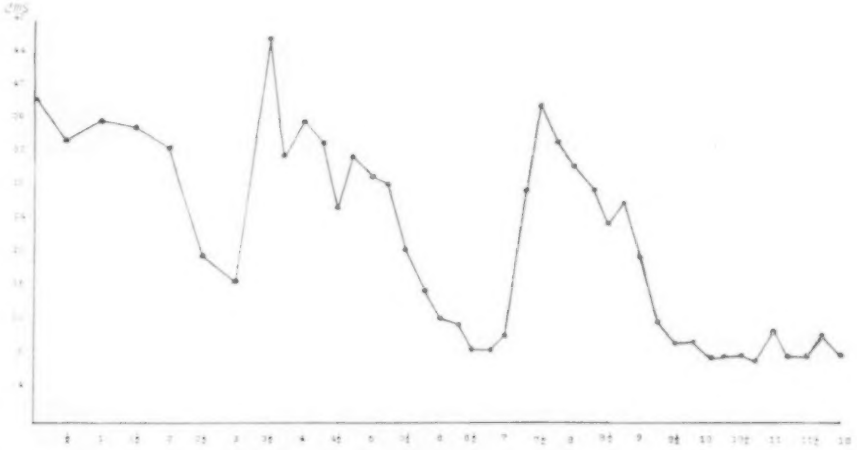

FIG. 9.—As in fig. 8 the bladder contained 20 oz. of fluid. Transverse lesion of 1st dorsal segment 35 days after infliction of the injury.

suddenly raising the pressure within the bladder, or by making the patient cough or strain. A rapid increase of tension on the walls of the bladder was evidently an effective stimulus.

It sometimes happened that during a contraction of the bladder the catheter was extruded and fluid escaped, often leading to complete evacuation. This frequently followed a series of contractions which culminated in one which raised the intravesical pressure to an exceptionally high level. It might be associated with reflex spasms of the legs and abdominal muscles excited by a stimulus to the lower limbs or to the perineal region, but it was then repeatedly observed that the contraction of the bladder and its evacuation followed the spasms of the legs and abdomen by a definite interval of time, sometimes by several seconds.

The following conclusions can be drawn from my observations. Immediately after a complete transverse lesion of the spinal cord at any level, or of the cauda equina, the bladder acts merely as an elastic reservoir and shows no signs of nervous activity. After a variable interval evidences of returning and gradually increasing tone of the musculature of the bladder-wall appear. Shortly after this the bladder becomes a reflexly active organ, at least when the lesion lies above the sacral segments of the cord.

No suitable apparatus was available with which to investigate the state of the sphincters, and such observations as were made add little to the general knowledge of their behaviour in acute spinal lesions. Within the first week or so of the onset of the paralysis a definite resistance was generally felt in passing the catheter through the sphincters, and there was usually no difficulty in keeping it in position or tendency for leaking to occur round it. It may be therefore assumed that at this stage, when the bladder was toneless, the sphincters preserve some tone. This corresponds with the fact that overflow incontinence generally develops later, and that it may be impossible to express urine during the first one or two weeks by pressing upon or massaging the bladder.

A little later, usually during the second or third week, it was often more difficult to keep the catheter in position and fluid escaped readily around it, indicating that the tone of the sphincter had become less. At this stage overflow incontinence was not uncommon. Later, when the bladder has regained tone, more resistance was experienced to the introduction of the catheter, and the sudden extrusion of the catheter and the evacuation of the bladder which often occurred, indicated that not only was the sphincter in a state of tonic contraction, but that it was also capable of reflex activity.

Attention may be drawn here to interesting observations published by Fullerton [2] on the state of the ureters and of the uretero-vesical sphincters early after the onset of complete transverse lesions of the cord, many of which observations were made on the same patients as my own experiments.

The ureteric orifices were inspected through a cystoscope after an intramuscular injection of indigo-carmine had been administered in order to observe more easily the urine issuing from them. Several cases with complete lesions of the cervical and dorsal segments were examined, and his conclusions were:—

(1) Peristalsis of the ureters continues, as evidenced by the rhythmical discharge of urine from them.

(2) Normal movements of the lips of the ureteric orifice take place, as shown by its visible systole and diastole.

(3) The tone of the uretero-vesical sphincter is maintained and the valve is competent.

It is obvious from these observations that the ureters and their sphincters behave differently to the bladder and its sphincters after the spinal cord has been damaged by a severe transverse lesion.

It is not intended to refer to the extensive literature on paralysis of the bladder, but the work of Head and Riddoch [3], published in 1917, deserves comment, more especially as some of the conclusions to which they came are not supported by my observations. This may be partly due to differences in the methods employed, for they measured only the amounts of fluid introduced into the bladder, not the intravesical pressure, and, as has been shown, there may be no close relation between them. My observations suggest that the intravesical pressure is a much more important factor in determining the activity of the bladder than the amount of fluid it contains.

Head and Riddoch described automatic emptying of the bladder as part of a "mass reflex" which could be evoked by stimulation of the legs and other parts below the level of the spinal lesion. They attributed this to "a vast outburst of motor energy . . . overflowing into visceral channels," or a wide irradiation of the reflexes due to loss of "local signature" in the cord.

Involuntary micturition was repeatedly observed and studied in the course of my experiments, and it certainly often followed spasms of the lower limbs which were either purposely excited or apparently spontaneous. My observations indicate, however, that the contraction of the bladder which occurred in these circumstances was not an immediate result of stimulation of the legs, but that it was due to the associated spasm of the abdominal wall which, by raising the intra-abdominal pressure, increased suddenly the tension on the vesical musculature.

The following facts point to this explanation: Evacuation of the bladder frequently followed a series of apparently spontaneous oscillations of intravesical pressure, which were usually not associated with spasms or other reflex movements of the lower limbs. It could also be produced by suddenly augmenting the pressure in the bladder by raising the reservoir of fluid in connection with the catheter, or by increasing suddenly the intra-abdominal pressure by coughing, deep breathing or a sudden compression of the abdomen.

When the lesion of the cord was sufficiently high flexor spasms of the legs were usually followed by, or associated with, vigorous contraction of the abdominal wall which must raise intra-abdominal pressure. If the intravesical pressure was observed under these circumstances it was seen that the contraction of the bladder did not occur simultaneously with the spasm of the abdominal wall, but after an interval, suggesting there was not an immediate overflow of innervation into the visceral centres in the cord. A short series of oscillations of pressure often preceded the more vigorous contraction which expelled the contents of the bladder.

The importance of abdominal spasm in exciting reflex micturition is well illustrated by a case described by Head and Riddoch [Case 8] in which scratching the right sole excited flexor spasms of the right leg, "a strong contraction . . . in the right half of the abdomen" and evacuation of the bladder; while on similar scratching of the left sole "the reflex movement was violent, but there was little or no movement of the abdomen" and "the energy evoked could not materially affect the activity of the bladder."

Further, though flexor spasms of the legs often extend to the abdominal wall, reflex extensor movements excited by peripheral stimuli usually do not do so, and they are less likely to be followed by reflex incontinence. Head and Riddoch in fact assert that "so long as extension can be obtained as a primary reaction energy does not overflow into visceral channels."

Finally, where the lesion lay so low in the cord that the reflexes excited in the lower limbs did not spread to the abdominal muscles, stimulation of the soles had no influence on the bladder.

From these facts it must be concluded that the evacuation of the bladder which follows stimulation of the lower limbs is not part of a "mass reflex," and that impulses arising from the periphery of the limbs do not spread to the spinal vesical mechanisms. The micturition which occurs under these circumstances is a result of the associated spasm of the abdominal muscles producing a sudden increase of intra-abdominal pressure; this augments the tension within the bladder and therefore excites it to contraction.

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THE STATE OF THE BLADDER AND ITS SPHINCTERS IN COMPLETE TRANSVERSE LESIONS OF THE SPINAL CORD AND CAUDA EQUINA.

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I.—Introduction.

Disturbances of micturition as a consequence of partial lesions of the spinal cord are frequently difficult to interpret in terms of current views of vesical function. We have elaborated a method of investigation of such disturbances, and our findings in a number of cases convinced us of the necessity of the examination of normal micturition and analysis of the disturbances following complete lesions of the spinal cord and cauda equina, before the analysis of partial lesions can be attempted. We have already described normal micturition [15], and here bring forward the outcome of our investigations of complete lesions.

A most complete and accurate review by Fearnsides [17] covers most of the literature of the subject up to that time. Since the subject is complicated, however, we shall first describe such work as appears to have direct bearing on our own problems.

The involuntary musculature of the vesical wall (detrusor) and of the internal sphincter receives innervation from two regions of the spinal cord. One innervation is derived from the lumbar sympathetic chain via the inferior mesenteric ganglion and hypogastric plexus (hypogastric nerves), the other from the sacral plexus by the pelvic nerves (sacral nerves or nervi erigentes). These two outflows intermingle in the vesical plexus of outlying ganglion cells and fibres which directly innervates the bladder and sphincter. The voluntary musculature surrounding the deep urethra (external sphincter) and the associated voluntary musculature of the perineum is innervated by the pudic (pudendal) nerves. Both the pelvic and the pudic nerves are derived from the second, third, and fourth sacral roots (Waldeyer [54], Head [26], Harman [25]), and corresponding segments of the spinal cord, while the hypogastric plexus through the sympathetic chain is derived from the eleventh and twelfth dorsal and first lumbar roots (Head [26], and Harman [24]), and corresponding segments of the cord. All three sources of innervation convey afferent fibres, amounting in animals to one-third the total number of fibres in the pelvic nerve, but only one-tenth in the hypogastric nerve [33, 34, 35].

Stimulation of the peripheral segment of the cut pelvic nerves in animals induces powerful contraction of the detrusor musculature with relaxation of the internal sphincter (Gianuzzi [20], Von Zeissl [59, 60], Elliott [16], and others). Stimulation of the hypogastric nerves causes contraction of the internal sphincter in all animals, including man (Learmonth [38]), accompanied by a degree of inhibition of the detrusor which varies with the species of animal employed (Elliott [16]). Stimulation of the pudic nerve contracts the external sphincter. Section of both pudic nerves in an otherwise intact animal leads to occasional slight incontinence [3]. Section of both pelvic nerves occasions a profound depression of micturition with an atonic distended bladder (Lannegrace [37], Elliott [16], Barrington [3]). This condition changes after a few days to intermittent micturition in small jets, each expressed only by powerful effort in the cat, and is further changed to intermittent spontaneous dribbling from a small bladder by later section of the pudic nerves (Barrington [3]). Subsequent section of both hypogastric nerves apparently has no effect on any of these disturbances

(Barrington). Section of the hypogastric nerves results in either no change [40], or but a slight frequency of micturition [3], and urine is still held at the internal sphincter (Barrington [3]). Section of all three sources of nerve supply is followed, after a short period of retention, by periodic discharge or "automatic micturition" (Dennig [14], Elliott [16], Wlasow [58]). The integrity of the pelvic nerves, therefore, appears of paramount importance to the adequate performance of normal, "voluntary" micturition.

Complete destruction of the lumbo-sacral segments of the spinal cord causes atony of the bladder with a resistant sphincter and resultant retention of urine. This state passes in the course of a few days to intermittent discharge from a small bladder (Goltz and Ewald [22] and Müller [41]). The effect is the same as that of combined section of both pudic and pelvic nerves. Goltz and Ewald observed that the subsequent state is one of intermittent automatic micturition. The detrusor musculature becomes remarkably hypertrophied.

Complete transverse section of the spinal cord above the lumbar segments in the dog and other animals is also succeeded, after a period of depression of function, by the development of a process of "automatic micturition." Large quantities of urine are periodically voided, each in a steady stream which almost or completely empties the bladder (Goltz [21], Sherrington [49]). Light momentary intermittent abdominal pressure, or stimulation of the perineum, facilitates its occurrence, strong stimulation of the reflexly active limbs causes it to cease (Sherrington [48, 49]). This automatic act in the spinal animal is accompanied by defæcation and a motor reflex in the tail [48]. Differences in level of section of the cord make no change in the development of the process. Barrington [3] states that in cats the external sphincter (compressor urethræ) is highly tonic in the period of depression and becomes less tonic as automatic micturition is developed, but in another place [7] states that this part of the urethra in the cat still retains resistance to outflow even when the pudic nerves are severed. In the spinal animal stimulation of the whole sciatic nerve is stated to cause micturition [51, 16], with relaxation of the internal sphincter [16], but this effect was not obtained from the internal pudic or small sciatic nerves [16]. Distension of the bladder has long been recognized as an adequate stimulus for reflex micturition [21, 23].

The effect of various partial sections of the spinal cord in animals indicates that the pathways controlling micturition travel in the most dorsal part of the lateral column, in the region of the pyramidal tract,

and that one such pathway on either side is alone sufficient to maintain control if the other be impaired [40, 9]. There is evidently much decussation of the fibres concerned in the lumbar and sacral segments [9, 51].

Barrington [3] describes five separate reflexes arising from the bladder and urethra and activating micturition. The first reflex is contraction of the bladder in response to increasing volume of contents, and the second secures strong contraction of the bladder when fluid forces the sphincter and runs through the urethra. Distension of the proximal urethra not sufficient to force the external sphincter causes a slight rise of vesical pressure and this forms the third reflex, while the fourth reflex is an active relaxation of the urethra when it is passively distended. By "urethra" he refers to the most proximal segment, which in the cat is surrounded by smooth muscle continuous with the neck of the bladder. There seems little objection to identifying the smooth muscle with what is ordinarily meant by internal sphincter. The fifth reflex secures relaxation of the external sphincter whenever the bladder makes response to distension. Barrington has shown that the first reflex has both afferent and efferent pathways in the pelvic nerves, for the second the pudic nerve is afferent and the pelvic efferent, for the third both pathways are in the hypogastric nerves, and for the fourth both pathways are in the pudic nerves. The fifth reflex has its afferent pathway in the pelvic nerve and efferent in the pudic nerve.

Barrington further states that the first reflex, the response of the bladder to distension, arises in the central nervous system at about the level of the plane through the posterior parts of the inferior colliculi dorsally and the middle of the pons ventrally [5, 4] and that the second reflex also completes its reflex arc in the brain-stem. The other three reflexes still occur in the spinal animal.

On the basis of the series of reflexes thus described the automatic micturition of the spinal animal remains unexplained except as a consequence of a leak past the internal sphincter. In a later paper, Barrington [8] describes a sixth reflex which is a relaxation of the plain muscle of the urethra by distension of the bladder after spinal transection. Thus some overflow might be expected from extreme distension, and this indeed is the condition of the "chronic" spinal cat as described by Barrington. It is, however, apparent to those who have worked with the reflexly-active spinal dog that forceful and apparently complete micturition can occur, and one must conclude that in this animal, which can be kept in the chronic spinal state with much greater ease and with much

fuller recovery of limb reflexes than the cat, vesical reflexes other than the third, fourth, fifth and sixth reflexes of Barrington are active.

In the decerebrate cat, Barrington [5] describes micturition as a forceful stream, each micturition terminating in a series of minor jets accompanied by perineal contractions. Stimulation of the perineum can provoke micturition. There is frequently some residual urine, and Barrington argues that decerebrate micturition is "inco-ordinate" on account of this lack of completion.

The effect of complete destructive lesions of the sacral segments of the spinal cord in man, as in animals, has long been recognized to be followed, after a period of retention, by automatic micturition (L. R. Müller [41], Bálint and Benedikt [2], Oppenheim [42], Schwarz [46], Adler [1]), which takes the form of "periodic incontinence" or "active incontinence ("active paralytic overflow" [12]). The bladder may become small and hypertrophied as in animals (Lhermitte [39]). After verified lesions of the conus there has been described a lack of natural desire for micturition, though involuntary micturition is often preceded for a few minutes by a feeling of tightening in the lower abdomen, and undue distension may cause pain [32, 41, 2]. It has been claimed that sense of distension of the bladder may remain unaffected (Riddoch [44]). No other function attributable to the intact hypogastric innervation of the bladder (D. 11—L. 2) has been demonstrated in these cases. Passage of urine can be secured by passive pressure or by a voluntary contraction of the abdomen by the patient [18], but apart from this there exists true involuntary automatic micturition which most usually takes the form of frequent discharge of small quantities of urine, but may develop into complete evacuation of a larger volume in a powerful steady stream five to six times a day [41, 2, 18]. A severe toxæmia is accompanied by gradual loss of automatic vesical function and redevelopment of complete retention [2]. This type of automatic micturition may be established following widespread destruction of spinal cord [11].

The occurrence of automatic micturition in man as a consequence of a complete transverse lesion of the spinal cord above the level of the sacral segments has also long been recognized [18]. When the condition is fully developed, large quantities of urine may be expelled by each micturition and the bladder completely emptied. The vesical pressure rises steeply during filling [1, 46]. When the bladder is filled a reaction occurs, as in the automatic bladder after conus lesions, but is here much more powerful, so that the vesical pressure often rises well over 100 cm. water pressure even with small volume of vesical contents (Frankl-

Hockwart and Zuckerkandl [18], Schwarz [46] and Adler [1]). This type of micturition has been distinguished as the "hypertonic bladder," as opposed to the relatively "atonic bladder" of automatic micturition following cauda equina lesions [18]. Though the stream is more powerful when micturition occurs from the hypertonic bladder, it is maintained that the discharge of urine is not easily obtained by steady pressure upon the abdomen, and a regular massage is necessary [18]. The sphincter offers resistance to catheterization, and estimation of the pressure necessary to overcome it shows usually that this is raised above the normal [39]. Percussion of the lower abdomen, on the contrary, facilitates micturition [18], as does also "reflex" stimulation [18, 42], such as passage of a catheter through the urethral meatus or stimulation of the glans penis. The height of segmental level of spinal transection has no relationship to the type of vesical disturbance resulting [55]. It has been maintained that the initial period of retention of urine in man is associated with powerful contraction of the internal sphincter (Rehfisch [43]). Though vesical contraction in response to filling is then usually absent, the detrusor is able to expel its contents through a catheter late in this period [27].

The "hypertonic" automatic bladder is often more difficult to catheterize than the less tonic automatic bladder following conus lesions, and it has been held by Müller [41] that the former type of automatic micturition differs from that following conus lesions only in the presence of effects attributable to the undue tonicity of the sphincters. The reaction of the "hypertonic" bladder to filling has been shown by Holmes [29] to be due to long slow fluctuations of vesical pressure which are more readily elicited as the phase of retention passes. Head and Riddoch [27], as a result of observations on the recovering reflexes in cases of complete transverse lesions of the spinal cord in man, found that at a certain stage of recovery elicitation of the flexion reflex facilitates discharge of the vesical contents through a catheter. This phenomenon occurred when the bladder contained less fluid than was required to stimulate automatic discharge, and was explained on a hypothesis of a spread of reflex effect in the recovering isolated segments of the cord, with resulting massive reflex discharge of flexion, micturition and sweating in response to any cutaneous stimulus, "the mass reflex." The teleological basis of this "primitive reaction" has been strongly criticized (Walshe [56, 57]). Schwarz [46] in his series of cases failed to elicit micturition by cutaneous stimulation.

The spontaneous fluctuations of vesical pressure originally observed

in the human bladder by Mosso and Pellacani [40], and in animal bladders by many investigators (Sherrington [47], Stewart [53], Elliott [16]), have been occasionally observed in manometric observation in work on the human bladder, and Holmes [29] has traced the emergence of rhythmical contraction during recovery from the depression of spinal shock. There has been, as far as we can ascertain, no analysis of the part played by rhythmical vesical contraction in vesical function.

Though in the course of our investigation we have subjected some twenty-nine patients to detailed investigation we have found only three lesions of the cauda equina and three spinal transections, with sufficiently discrete and complete lesions, of sufficiently chronic nature to demonstrate their constancy, and of sufficient duration of recovery from the effects of shock to give evidence of the fundamental principles underlying the disorders.

II.—Method.

The primary object of the present investigations has been to seek information as to the exact form of vesical activity and correlated sphincteric disturbance in spinal lesions and the relationship of these to the phenomena readily observed clinically. For this purpose records of the vesical and urethral pressures during micturition were chosen as indicative of the phases of vesical activity.

Records of vesical pressure have been made by a technique which has been described in detail in our earlier communication [15] of control experiments in normal bladders. The method consists of the introduction of two catheters so that a narrow catheter lies within the lumen of an ordinary rubber catheter. Through one the bladder is filled with sterile warm saline, and the vesical pressure is recorded by mirror manometers connected to each catheter. Subsequent withdrawal of the larger catheter into the urethra allows the registration of the discharge through the sphincter to be made by the manometer of this catheter while vesical pressure is concurrently recorded by the other. It was found necessary to record intra-rectal pressure and movements of the abdominal wall and the perineum concurrently in order to estimate the effect of extravesical changes. The records were made on a slowly moving strip of bromide paper by the beams of light reflected by the manometers. Time is recorded by a rotary time marker showing one-fifth second intervals. To avoid overlapping of records the manometers recording rectal and abdominal pressures are arranged to show a down-

ward deflection for increase of pressure on the balloons, the other tracings make upward movement for increase of pressure.

In recording discharge of a sphincter the urethral catheter connection is allowed to leak through a narrowed side opening. The column of fluid in the catheter records the impact of discharge of even one drop of urine with very brief latency (some 0·01 second).

Our own method, on account of the numerous controls necessary and the bulk of apparatus required for long running records, is not readily applicable at the bedside. In its essential principle of measurement of the vesical pressure, however, we believe that all the data bearing on the vesical pressure may be readily observed by more portable apparatus such as was used by Gordon Holmes, or by the portable cystometer introduced by Rose [45, 45A], provided that the rate of filling with such apparatus is slow, and adequate time given for adaptation of pressure to volume. A number of the smaller fluctuations will be observed only with difficulty in a mercury manometer.

We have not had access to patients in the early stages of complete lesions. The work of Gordon Holmes, published in the preceding paper in this Journal [29], carried out also by measurement of vesical pressure, surveys disturbances at this period, and provides us with the necessary perspective.

III.—The Reaction to Distension.

Allowing the bladder to fill slowly from a reservoir brings about a gradual rise in the vesical pressure which reflects the resistance offered to the entering fluid by the musculature of the vesical wall. In order to estimate the power of adaptation of the bladder to the volume of its contents our usual procedure was to close the inflow after the introduction of each 100 c.c. of fluid and for an interval to record the behaviour of the bladder at constant volume before allowing the next 100 c.c. to enter. The fluid was introduced slowly through a narrowed orifice under a steady pressure of 50 cm. reservoir level height. The rate of filling, unless expressly stated otherwise, is slow (see figs. 8 to 13) but is not constant owing to the variable resistance to inflow provided by slight differences in the apertures of different catheters and the pressure of vesical contents. The narrow catheter materially lessens the aperture of the larger catheter through which it passes. The clinical state of the patients is described in the Appendix.

(1) *The Effect of Lesions of the Cauda Equina.*

In comparison with the bladder of a normal subject the vesical pressure in Case 1 mounted rapidly as volume increased, so that at a volume of 200 c.c. it had reached 70 cm. of water (fig. 1). The rise of pressure was at first regular (fig. 8 A) but as the volume was maintained at 100 c.c. a series of fluctuations of pressure made their appearance in groups of two and three (fig. 8 B), associated with discomfort. These reappeared after increasing the volume to 150 c.c. (fig. 8 D), and again at 200 c.c. (fig. 9 A). It will be observed that each filling evokes a smooth rise of pressure which subsides, or "adapts," when the volume is maintained constant. The waves of pressure, which are quite distinct from the respiratory and other fluctuations of abdominal pressure, and only once related to a rise of rectal pressure (fig. 8 B), are undoubtedly of vesical origin and are waves of vesical contraction. At the higher volumes the waves emerge from the steadily mounting resistance of the bladder to distension. The subsequent adaptation of this resistance to any given volume, well seen in the graph, fig. 1, reveals the origin of the resistance in active vesical contraction evoked by distension. The resistance, when examined by brief fillings, gathers momentum up to a point, after which, whether filling is continued or not, there is a pause followed by the appearance of waves of vesical contraction (cf. fig. 8 C and 8 E). If filling is not interrupted the resistance usually mounts steadily and waves of pressure appear as soon as the resistance reaches its maximum (figs. 2 B and 9 D). The more rapid the filling the higher is the rise of tonic resistance for equivalent volumes (fig. 2 A). Emptying in small amounts does not disturb the rhythm of vesical waves (fig. 9 B), and if in large amounts lowers the pressure rapidly (fig. 9 C), and waves of contraction lessen rapidly in amplitude (fig. 9 E). No fresh vesical contraction was observed to be stimulated by emptying.

In Case 2 the curve of pressure rose more slowly as the volume increased (fig. 3) and approximated more closely to the normal. The pressure reached 18 cm. water at 400 c.c. during one filling. A regular series of small waves of pressure early made their appearance (fig. 10 A), and later appeared in groups (fig. 10 B and C) as in Case 1. Emptying the bladder had precisely the same effect as in Case 1.

In Case 3 the rise of vesical pressure was steeper (figs. 4 and 13 A) as in Case 1, reaching 29 cm. at 200 c.c. and 46 cm. at 300 c.c., but spontaneous fluctuations were only faint and occurred for only a short period at a volume of 200 c.c. during filling. They appeared also at

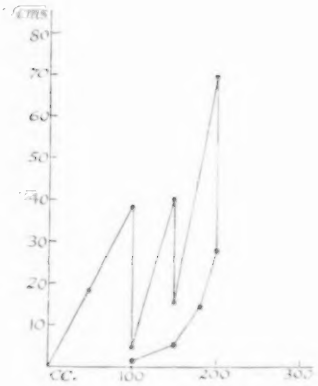

FIG. 1.

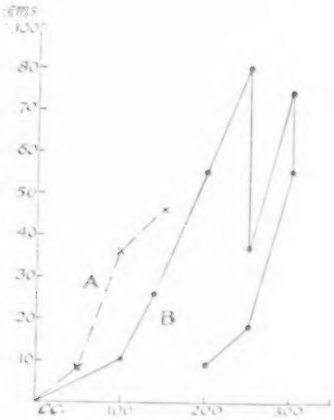

FIG. 2.

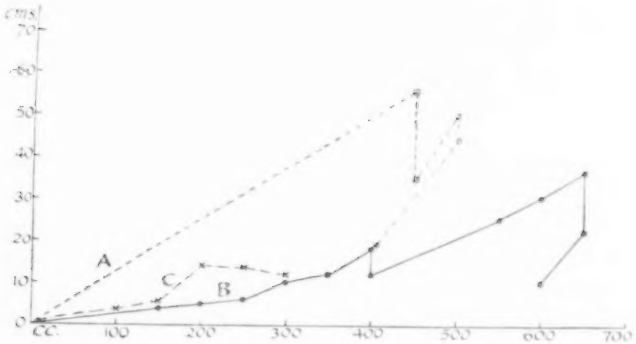

FIG. 3.

FIGS. 1 to 7.—Graphs of relationship of intravesical pressures and volumes plotted from continuous records during distension of the bladder. In figs. 1, 2 B, 3 A and B, 4, and 7 A, the curve is continued backwards through the same volumes to show the pressure during subsequent emptying. Adaptation of pressure to a relatively steady value, whenever the volume was maintained constant for a period, is plotted as a vertical line.

FIG. 1. *Case* 1.—From records of slow filling, part of which is shown in fig. 8. Reservoir height 50 cm. to 100 c.c. and from then onwards 100 cm.

FIG. 2. *Case* 1.—Broken line A from record of very rapid continuous inflow at 100 cm. reservoir height. Fluid commenced to flow around catheter at 150 c.c. B, Graph of continuous inflow at intermediate rate at 100 cm. reservoir height. (See fig. 9 D.)

FIG. 3. *Case* 2.—From three different experiments. A, October 15, 1932. Continuous inflow with reservoir height 100 cm. B, November 13, 1932. Filling with reservoir height 50 cm. (See fig. 10 E.) C, November 27, 1932. Slower distension, reservoir height 100 cm. (Fig. 10 A, B, C and D.)

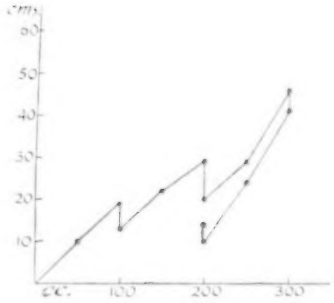

FIG. 4.

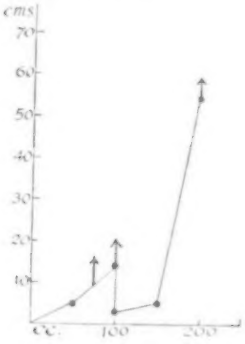

FIG. 5.

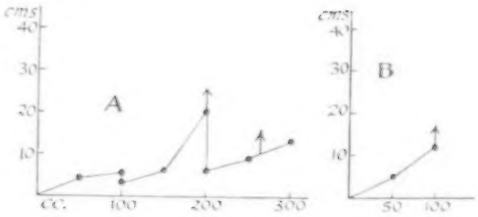

FIG. 6.

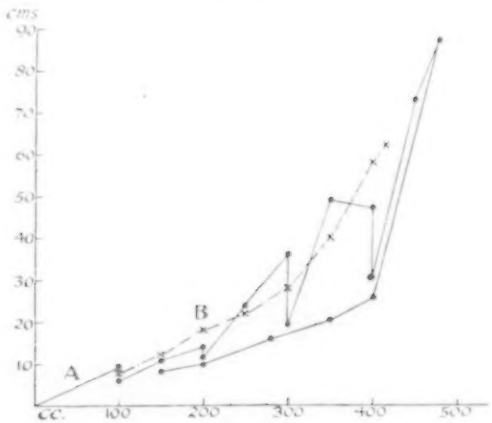

FIG. 7.

FIG. 4. *Case* 3.—August 27, 1933. Reservoir height 50 cm. Slow filling, part of which is shown in fig. 13 A.

FIG. 5. *Case* 4.—February 18, 1933. Filling to 150 c.c. at 50 cm. reservoir height and from 150 to 200 c.c. at 100 cm. reservoir height. Arrows represent the occurrence of isolated spontaneous vesical contractions. (See figs. 11 A, B, C and D.)

FIG. 6. *Case* 5.—A, May 29, 1933, 50 cm. reservoir height (fig. 12). B, August 29, 1933. Rapid filling. Reservoir height 50 cm. Immediately after inflow closed at 100 c.c. a large spontaneous contraction reached 130 cm. pressure.

FIG. 7. *Case* 6.—September 30, 1933. Continuous line A from record with reservoir height 50 cm. to 400 c.c., 100 cm. to 478 c.c. (latter portion of record in fig. 13 E). Broken line B shows continuous filling at slow rate. Reservoir height 100 cm. (fig. 13 B).

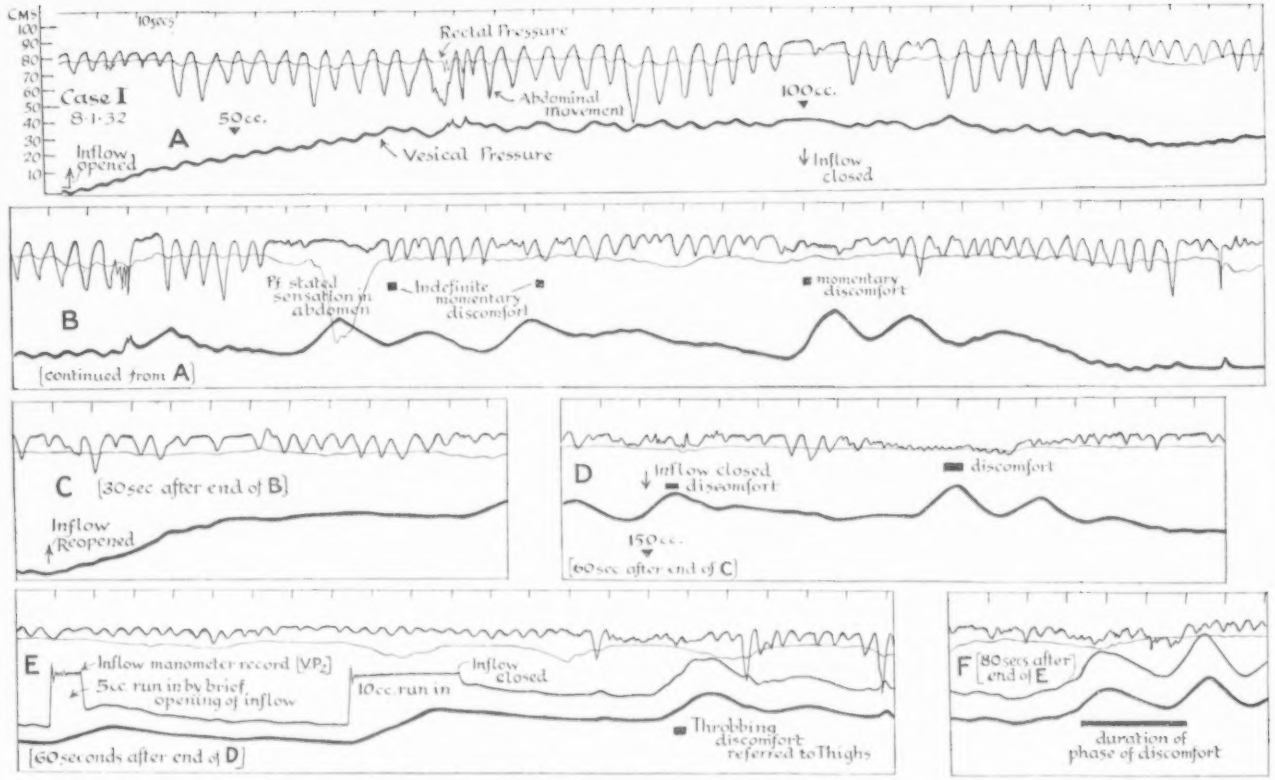

FIG. 8. *Case* 1.—Tracings from record of vesical pressure showing reaction to distension. Reduced to $\frac{2}{3}$.

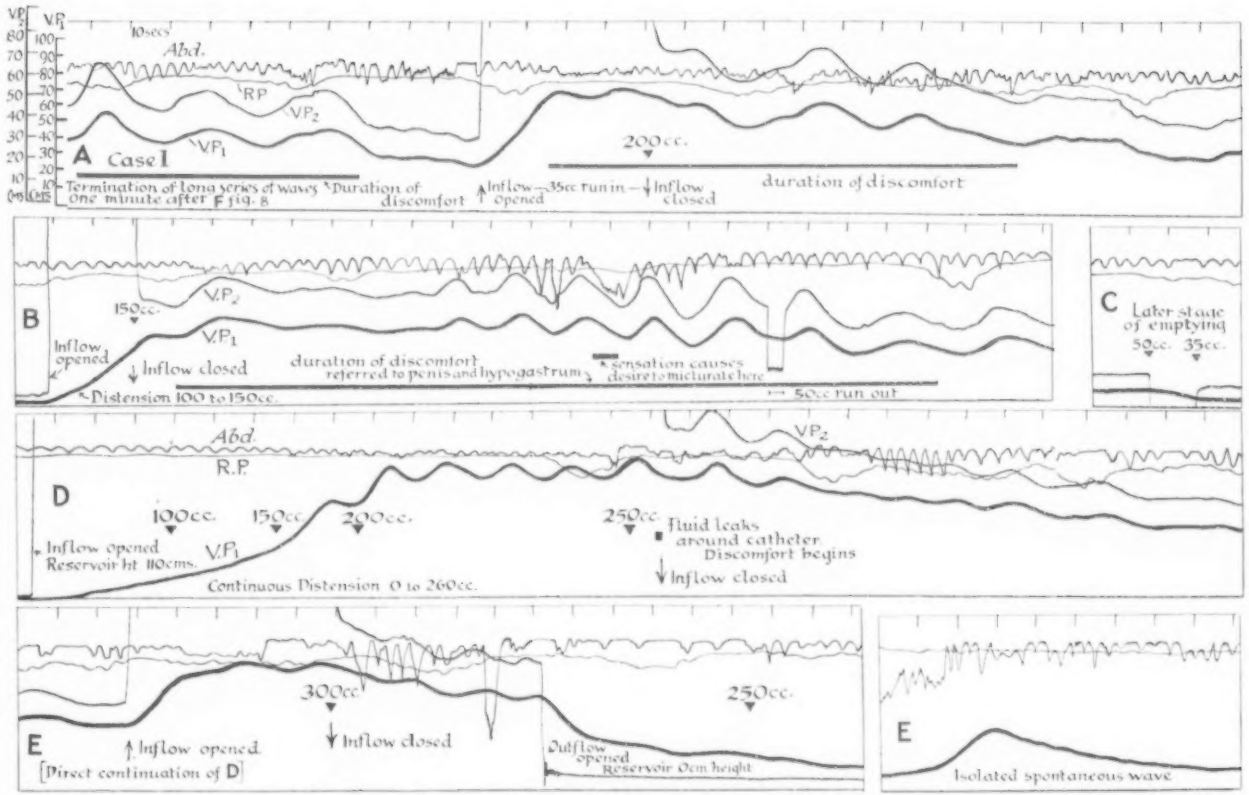

FIG. 9. *Case* 1.—Further excerpts from the same experiment as in fig. 8. A begins one minute after fig. 8 F. Volume in E 140 c.c.

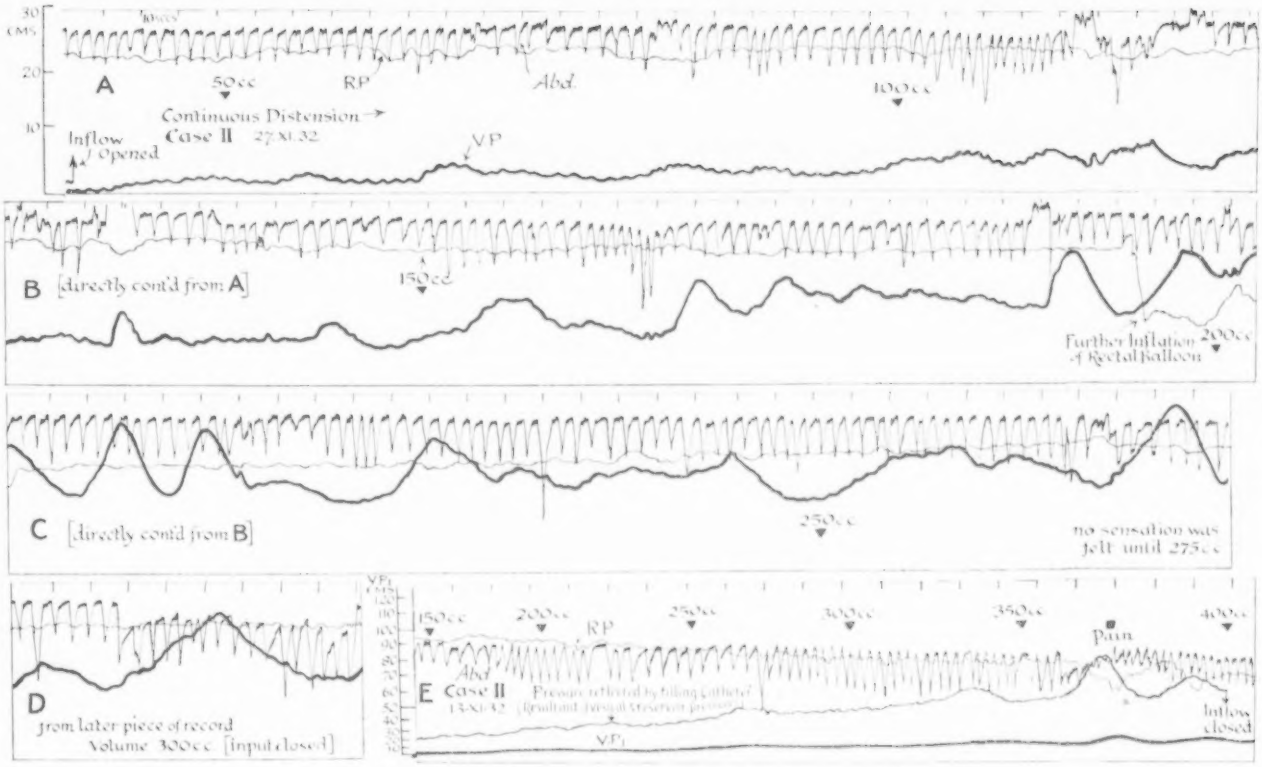

FIG. 10.—From records of Case 2. Vesical pressure during continuous distension.

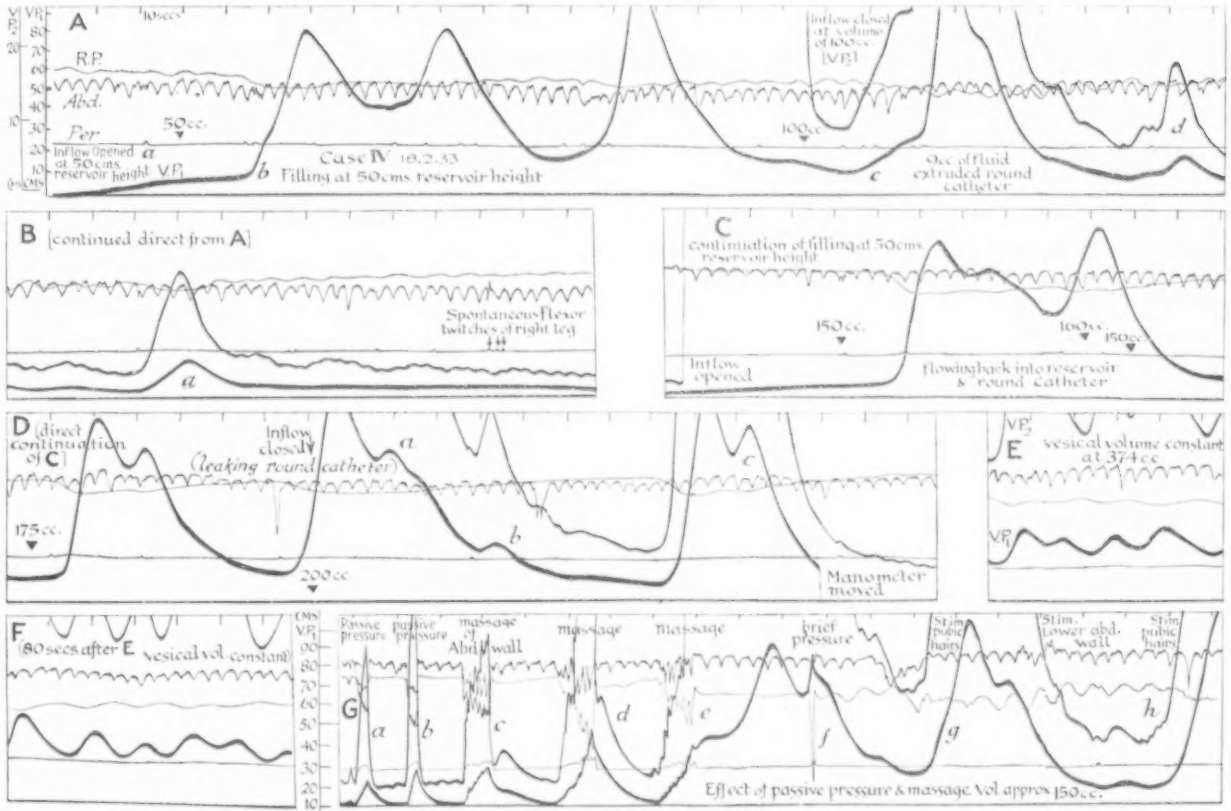

FIG. 11. *Case* 4.– A, B, C, D, E and F show reaction to intermittent distension. G illustrates effect of extravesical stimulation.

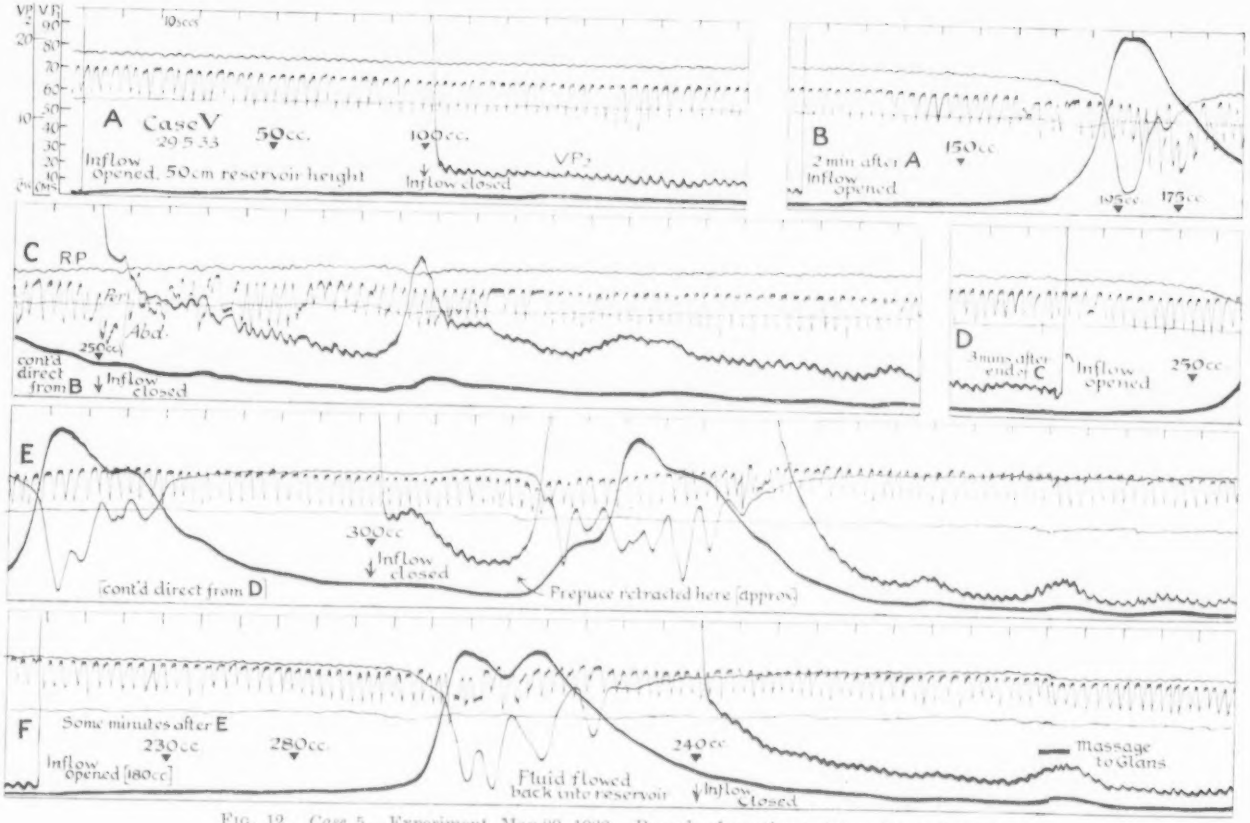

FIG. 12. *Case 5.* Experiment, May 29, 1933. Records of reaction to intermittent distension.

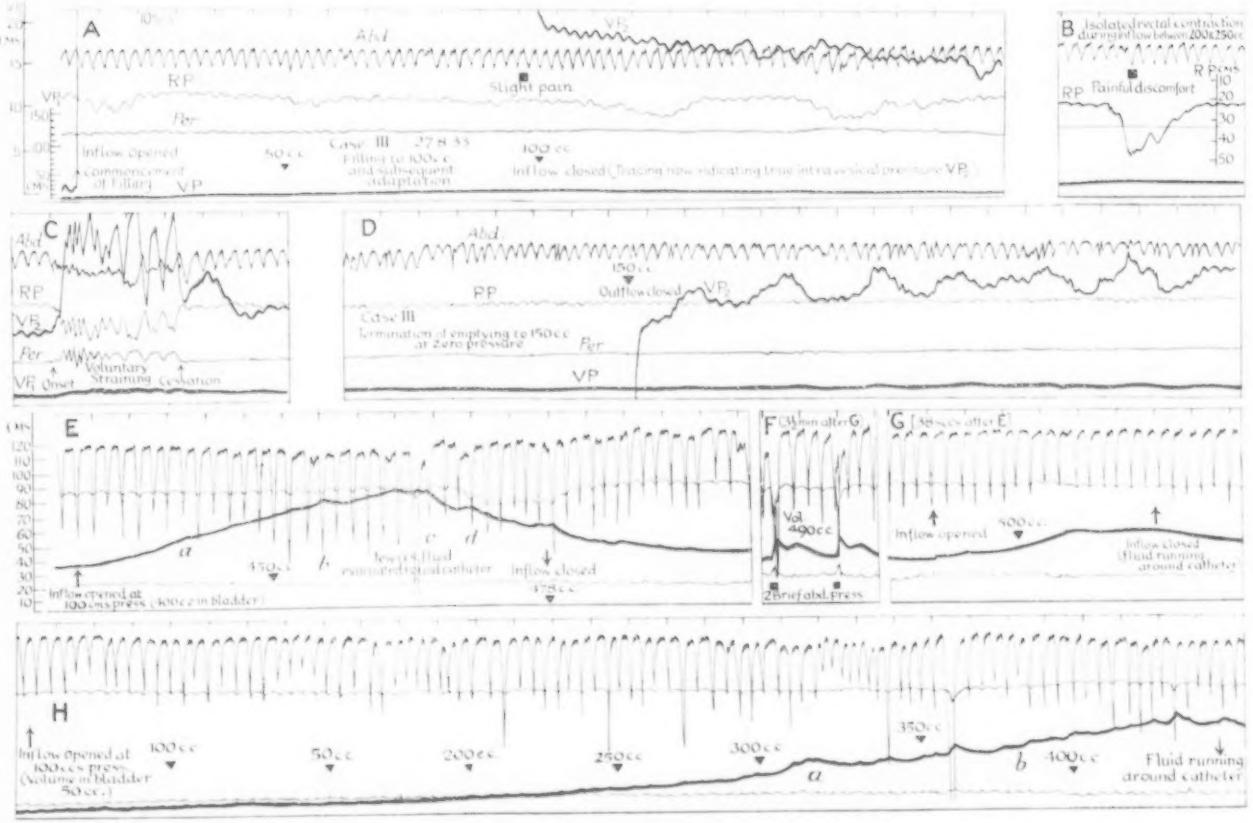

FIG. 13.—A, B, C and D, are excerpts from records of Case 3, and E, F, G and H from Case 6.

a volume of 150 c.c. (fig. 13 D), as the pressure rose following a period of emptying.

Variation in the manner of distension alters the reaction. For example, in Case 1 a continuous inflow, increased in rate by raising the reservoir pressure to 100 cm. water, induces a steeper pressure curve (fig. 2 A) than that obtained under our usual conditions (fig. 1), accompanied by similar though not earlier stimulation of spontaneous fluctuation. Refilling the bladder after a long period of distension at high volume gives a lower pressure throughout (figs. 3 B and 10 E).

In these bladders the process of adaptation of pressure to any constant volume is highly developed. In fig. 1 it will be seen that this resting value at each volume is often only slightly higher than the pressure at equivalent volume as the bladder is emptied. During the process of distension there is therefore evoked an increment of resistance of the vesical wall which is added to what may be taken as that due solely to the passive elasticity of the organ. This increased resistance to filling is the greater as speed of filling is increased. The manner and degree of its development strongly suggests an active tonic reaction of the bladder in response to *increasing* tension on the vesical wall, which commences to subside immediately the volume is kept constant.

A sudden passive rise of pressure such as is produced by a momentary pressure on the bladder through the abdominal wall in each of these

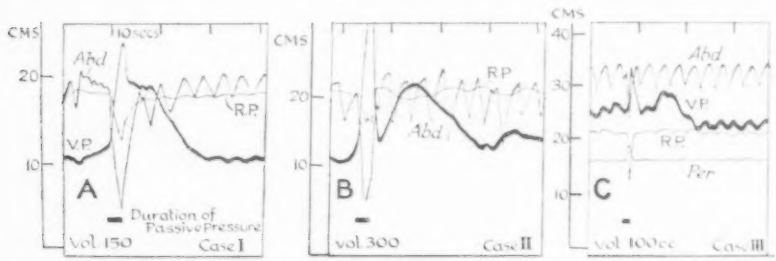

FIG. 14.—To show the vesical contraction stimulated by brief passive pressure on the bladder in each of the three cases of cauda equina lesions. The duration of the passive pressure is indicated by a horizontal black line. Reduced to ½.

cases is followed immediately, or at an interval of up to two seconds, by the onset of a small low wave of increased pressure (fig. 14). The pressure had to be rapidly applied as well as brief in duration. The reaction of the bladder to distension is thus "sampled" by a brief stretch, and is therefore revealed in phasic as well as progressive effect. This

delayed wave is also seen after the last of a series of pressures (fig. 13 c) but is not in the nature of a physical effect, for an equivalent or larger fall of pressure following upon a prolonged *steady* pressure never elicits it. The secondary contraction, as we shall refer to it, follows only brief pressure and is the result of some stimulus during the onset of the pressure.

The spontaneous waves of vesical pressure in this type of lesion were usually fluctuations of the same duration as the response to brief stretch, and we regard this as the single contraction of the bladder, analogous to the "twitch" of striped muscle. In Case 1 and Case 2 a larger, more prolonged wave, compounding several such small waves, appeared spontaneously at intervals (fig. 9 E). In Case 3 no such fused large contractions occurred. Apart from a rapid imposition of pressure upon the bladder through the abdominal wall, no external stimuli provoked any evidence of vesical activity.

(2) *The Effect of Complete Transverse Lesion of the Spinal Cord.*

As with the bladders after lesions of the cauda equina we have not been able to examine the first stage of complete retention of urine. The following description applies to the stage of recovery of reflex activity by the divided spinal cord. The reaction of the bladder to distension was powerful in Cases 4 and 5. The vesical pressure, as may be seen from the graphs (figs. 5 and 6), rises steadily but only moderately steeply, to reach 5 to 14 cm. water at 100 c.c. In each case the process of filling appeared to excite remarkably powerful and prolonged contractions of the bladder, reaching over 100 cm. pressure (figs. 11 and 12) lasting some thirty to sixty seconds and relaxing to, or near, the preceding pressure although filling was continued. These large isolated responses occurred at volumes as low as 75 c.c. in Case 4 and 120 c.c. in Case 5. If filling were continued they occurred in a series at intervals of one to one and a half minutes (figs. 11 A, *c* and *d*), but gradually grew smaller and less frequent as the volume became greater than 300 c.c. (Case 4) or 250 c.c. (Case 5), now giving way to a continuous series of small waves (fig. 11 E). These small waves at high volumes are of greater regularity and brisker frequency than those above described in the bladder after lesions of the cauda equina.

If the volume were kept constant after the appearance of a large wave, the disturbance was found to settle down slowly with the appearance of smaller waves in diminishing series (figs. 11 A, B and D, and fig. 12 c). The records of these waves at constant volume (isometric)

reveal superadded smaller fluctuations, as in fig. 11 A at *c*, and 11 D at *a*, *b*, and *c*, and their persistence throughout the large wave on some occasions, and disappearance in the trough, is interpreted as evidence that the large prolonged responses are compounds of such small single waves, here imperfectly fused.

Diminution of the volume of vesical contents by releasing the outflow resulted in a steady fall of vesical pressure. If the outflow were rapid any contractile activity which was previously present disappeared forthwith; if slow both frequency and amplitude of contraction rapidly diminished. On no occasion did diminution of volume stimulate vesical contraction. The low pressure during emptying reflects only the passive elasticity of the organ. If the outflow were closed after discharge of any volume of vesical contents the pressure remained very low, approximating to that of the inactive bladder at that volume, and contractile activity gradually reappeared only after an interval.

The large isolated contractile reactions which form the prominent feature of the fillings of Cases 4 and 5 are evoked by distension of the bladder. The tension of such contractions appears to be in the region of the greatest of which the bladder is capable and for that reason we shall term them "maximal" responses. They may be likened to the motor tetanus of striped muscle. The introduction of small volumes of fluid reveals that a certain definite volume of increase is required to elicit them. For example, in Case 5, a contraction of this type having been allowed to subside, fluid was run into the bladder at high input pressure in varying amounts, and 7 c.c. and 14 c.c. were each unsuccessful. Though each was accompanied by a rise in the intravesical pressure this rise commenced to diminish as soon as the inflow ceased. On the introduction of 16 c.c., however, the vesical pressure rose more steeply with the last 4 c.c. and, despite cessation of inflow, mounted with increasing steepness to form the ascent of a large isolated wave of contraction. The resistance of either lumen of the double catheter being large, an especial experiment was devised for the sudden introduction of 1, 2, 5, 10 c.c. of fluid by means of a syringe and single catheter in subject 5. This manœuvre was ineffective in eliciting contraction even when 10 c.c. fluid was introduced within one second, or introduced and withdrawn within two seconds. The rise of vesical pressure corresponding to the introduction of 10 c.c. at an existing volume of 100 c.c. is small. It will be clear, however, that the reaction to distension is not so much a matter of volume as of increase of stretch. For example, it is seen in fig. 11 that though a maximal contraction was evoked by filling to 100 c.c. in

Case 4, if this were allowed to subside further filling elicits a maximal contraction only when the volume is approaching 200 c.c. (fig. 11 C). In Case 5 the same latency of reaction is found if one reaction were allowed to subside (figs. 12 D and F). The stimulus for the reaction is increment of stretch of the wall of the bladder.

In a different manner, probably depending upon the speed of acceleration of tension, a sudden stretch of the bladder evoked by a momentary passive pressure on the lower abdomen regularly elicits vesical contraction. This takes the form of a single wave of vesical pressure, commencing within two seconds after the onset of the brief stretch (fig. 15, and figs. 28 and 29, Plate XV). The duration of this contraction

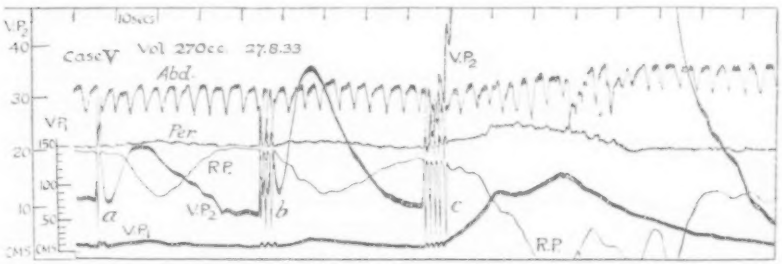

FIG. 15. *Case 5.*—To show the summation of the effect of repeated brief passive pressures on the bladder at constant volume. At *a* one brief pressure is applied and released, at *b* three, and at *c* five such pressures are imposed in rapid succession. The lowest curve ($V.P._1$) shows the vesical pressure recorded by a manometer much less sensitive than that which gives the record $V.P._2$. The rectal pressure (R.P.) also shows induced waves of rectal contraction. Reduced to $\frac{1}{2}$.

is that of the smallest spontaneous wave observed in the same bladder (fig. 29 B) and, as in the bladder after cauda equina lesion, we may regard it as a single or " twitch " contraction. It was found that an exceedingly brief, though powerful, pressure was not effective or produced only a very slight secondary contraction (fig. 29 A), whereas slightly longer pressures, reaching a maximum and declining to complete release in from 0·5 to 1·5 seconds, were the most effective (fig. 29 B). Provided that the pressures were gentle and sufficiently rapidly made the response varied in maximum tension, but not in duration, with the degree of pressure exerted (fig. 28). More powerful pressure, even if brief, induced a more delayed and flattened response (fig. 29 C), Slower pressures occasionally produced a similar wave of contraction but were more often ineffective (fig. 11 G). Repetition of passive pressure during the latent period, if light, appeared not to delay the

appearance of the contraction, which was larger in proportion to the number of pressures applied (fig. 15). Heavier pressures were either without effect or delayed the phenomenon until after the last pressure of the series (fig. 28). More frequent repetition of pressure also impaired the development of contraction during stimulation. The response to brief stretch is thus much more readily elicited from these bladders and develops much greater tension than in those isolated by cauda equina lesions. Such increases of abdominal pressure which accompany a cough, a sigh, or a deep breath are effective in evoking this contraction wave with its characteristic latency. As in Cases 1, 2 and 3, moderate pressure suddenly applied, maintained for a period and then released, is not followed by any secondary contraction (fig. 11 *c* at *a* and *b*). The stimulus for the vesical contraction is the increase of pressure. The delay in appearance of the contraction after the last of a series of pressures, as in fig. 28, at *d* and *g*, therefore cannot mean that the contraction is stimulated by the fall in tension, but that it is the result of the last increase of pressure of the series. The earlier pressures in the series must also produce contractions which are impaired by subsequent stretch, but when the pressures seem to produce greater effect, as in fig. 15 at *b* and *c*, the tension is found to be already rising between the later pressures.

If the passive pressures upon the bladder were long enough repeated a large isolated maximal contraction, such as is evoked by filling, is readily elicited (fig. 15 *c*, fig. 28 at *a*, fig. 30 at *b*). The transition from small waves to large response is, however, not smooth, and the induced secondary wave, having reached a plateau or "step," fails to decline, and the tension commences to rise again, passing into a "maximal" response (figs. 28, 30). If the series of pressures were prolonged no transition was observed (fig. 33). The contraction directly induced by single brief passive pressure and by a short series of such pressures, appears of comparable size and ease of elicitation whatever the volume of vesical contents. The passage of such a contraction into a "maximal contraction" is facilitated by distension of the bladder and is readily provoked at volumes approaching that at which such a reaction tends to occur spontaneously. That volume is not, however, the only deciding factor in the appearance of the transition is revealed by the slight differences which decide its elicitation at a constant volume. In fig. 28, two contractions are induced by a series of light pressures, at *a* and *d*, the larger of which passes into a maximal contraction. Similarly, in fig. 30, of two similar contractions the greater, *b*,

stimulated by slightly more intermittent pressure, leads to transition to a maximal contraction. A certain degree of active contraction must be stimulated before the transition will take place. Active contraction provoked by distension can replace in part that required to be produced by passive pressures, which then make transition to maximal contraction more readily. There was found every possible combination of the secondary effect of passive stretch and the active contraction produced by increasing volume. The maximal contraction at *e* in fig. 11 G is in fact identical in mode of production with that at *b* in fig. 11 A. In each case active contraction of the detrusor is brought to such a level that it appears to become self-stimulating and thus explosive.

Once a maximal contraction is elicited by this crisis of self-stimulation it does not persist, but disappears after a fairly constant period only to reappear after another period, so that rhythm occurs. It has been shown that continuous stimulation of the pelvic nerve in animals evokes a rhymical contraction of the detrusor [53]. The mechanism of rhythm production is here apparently identical with that of the heart and of spinal reflexes such as the scratch reflex or reflex stepping, and involves the little understood development of "refractory phase."

In Case 4, the more rapidly the bladder was filled the lower the volume at which a reaction occurred, a relationship well known to earlier workers [18]. This relationship was less prominent in Case 5.

The large explosive "maximal response" was in Case 5 invariably accompanied by a rise of rectal pressure which commences a few seconds later than the rise of vesical pressure (figs. 12 and 30). After mounting steadily, the rectal pressure then breaks into rhythmical fluctuations, showing partly fused small contractions at intervals of approximately ten seconds, and gradually subsiding as the vesical contraction passes away. The rise of pressure is not so prominent in Case 4, though waves of rectal pressure, of rhythm entirely different from abdominal and vesical movements, occur (figs. 11 G *g*, and 11 A *c*). Small rectal contractions were rarely observed and were elicited by brief pressures, very rarely as a delayed effect of abdominal pressure (figs. 15, fig. 28, and fig. 29 D at *a*). Isolated rectal contractions were also occasionally seen in Cases 1 and 2 (fig. 32 B).

Case 6, who was in a state of advanced toxæmia, exhibited a different response to distension of the bladder. The vesical pressure rose gradually to 16 cm. water at 200 c.c. (fig. 7) and small slow fluctuations appeared. The pressure rose rapidly at 300 c.c. and 400 c.c., but not until 450 c.c. was reached did a reaction with small superimposed spontaneous

fluctuations occur (fig. 13 E). The pressure had mounted evenly to 73 cm. water and began to fluctuate (fig. 13 E at *a*, *b*, *c* and *d*), with escape of some drops of fluid around the catheter. After an interval, during which this reaction subsided, further filling evoked another similar reaction at a volume of 500 c.c.

These reactions presented a much more gradual transition from the tonic contraction of the bladder than did the high resistances of Cases 4 and 5, but fused waves were present. A brief pressure evoked no recognizable secondary contraction at volumes of 100 c.c. and 200 c.c., a small secondary contraction occurred after each pressure at 300 c.c., and a much more pronounced contraction at a volume of 400 c.c. (fig. 13 F). A series of powerful passive pressures upon the bladder did not succeed in inducing any larger response. The detrusor in Case 6, therefore, reveals the essential phenomena seen in Cases 1, 2 and 3, and lacks the large explosive maximal responses found in Cases 4 and 5.

IV.—Disturbances of Function of the Sphincters.

(1) *The Effect of Lesions of the Cauda Equina.*

The clinical disturbance of micturition complained of by the patients in this group was in two cases (1 and 2) an intermittent spontaneous passage of urine accompanied by an unpleasant sensation which caused the patient to attempt to assist its passage by straining. Both patients could usually commence micturition by straining. In Case 3 there was uncontrollable dribbling micturition increased by any bodily movement, and also ability to pass urine by voluntarily straining the abdomen. None of these patients was able to restrain a spontaneous micturition during its progress.

The method of registration of discharge from the sphincter was by withdrawal of a larger outer catheter until vesical pressure ceased to register, as we have described in detail elsewhere [15]. A leak was then allowed in the manometer system of the outer catheter so that a rise of pressure in the associated manometer tracing (labelled U.M. in illustrations) revealed the onset of discharge of fluid beyond the sphincter and also a fall of pressure immediately closure of the sphincter commences. The inner catheter remained within the bladder, and its manometer recorded the changes in vesical pressure (V.P. in illustrations).

Spontaneous micturition is readily evoked by increasing distension. Analysis of the records of Cases 1 and 2, in whom well-defined spontaneous micturitions were observed, reveals discharge of urine occurring

during the course of spontaneous fluctuations of vesical pressure such as were observed in these bladders in the course of the reaction to distension. The discharge accompanied waves which were in every instance

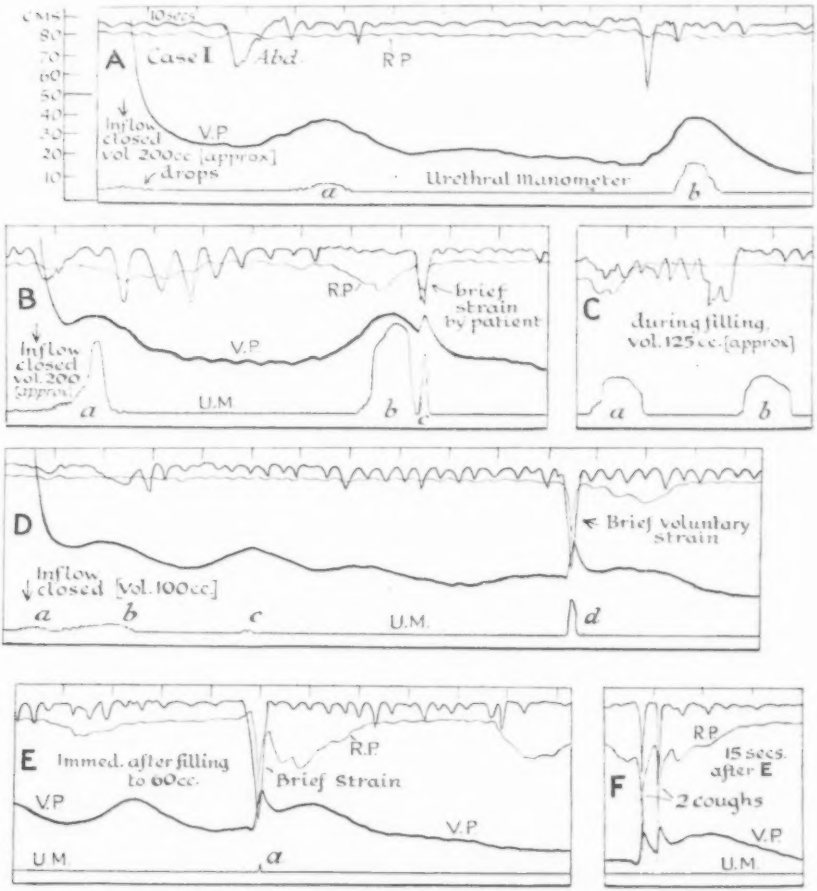

FIG. 16. *Case* 1.—Spontaneous micturition resulting from distension of the bladder. In records A, B and D the inflow was shut off as the first few drops of discharge were observed to pass through the urethral catheter, and from that time onwards true intravesical pressure is recorded by the manometer, V.P. The pressure of discharge is recorded by the urethral manometer, U.M. Reduced to ½.

longer in duration than the smallest waves during distension and longer than the waves induced by brief stretch. They were exactly comparable to the waves shown in figs. 9 E and 10 D. The sphincter opens at intra-

vesical pressures varying from 24 to 30 cm. in Case 1 (fig. 16), and 18 to 23 cm. in Case 2 (fig. 18), and closes at a slightly lower value. At times the sphincter remained closed with a vesical contraction reaching a slightly higher pressure (e.g., 31 cm.) than that at which it had opened just before (e.g., 27 cm.). The closure of the sphincter occurred at a vesical pressure just above that at which it had opened. Commencement of discharge is gradual, with early acceleration, so that the later part of the opening may be abrupt (figs. 16 B, C, and 18 B). The main portion of discharge reflects the pressure of the accompanying vesical contraction. Closure of the sphincter shows the same sinusoidal curve as is seen in its opening, and the discharge is often symmetrical. On some occasions the sphincter opened gradually but closed in a more decisive fashion (fig. 16 B, *a*). The commencement of spontaneous discharge was always secondary to a spontaneous rise of vesical pressure of wave form.

Accompanying many responses a respiratory arrhythmia of much longer duration, with little resultant change in intra-abdominal pressure, revealed the tendency of the patient to make straining movements of the abdomen to hasten micturition in order to attempt to abolish the unpleasant sensations arising with the spontaneous vesical contractions. The patient found it difficult to suppress this movement. The intra-rectal pressure curves show only the sporadic changes which continued independently of micturition and were not modified by its occurrence.

In Case 3 no defined automatic evacuation of fluid occurred during experiment. Although spontaneous waves of vesical contraction occurred at intervals they were of small amplitude and duration. At a vesical volume of 200 c.c. fluid escaped past the sphincter in a continuous series of drops at intervals of approximately five seconds. There was no large accompanying fluctuation of vesical contraction. The manometer used in recording vesical pressure at this time was not sufficiently delicate to establish the presence or absence of the small waves of vesical pressure seen during distension in this patient.

When Cases 1 and 2 were instructed to attempt voluntary micturition the intra-abdominal pressure was raised by voluntary contraction of the diaphragm and abdominal wall. The rectal and vesical pressures rose steeply (fig. 17, fig. 32 A, C, D, E and fig. 18 D at *a*). Discharge commenced when the vesical pressure had reached 27 to 53 cm. of water in Case 1, and 26 to 28 cm. in Case 2. The higher the vesical pressure immediately before the effort the lower was the pressure at which the sphincter opened during the effort. The decline of the pressure of

discharge following a rapid cessation of straining was usually at first gradual, with delayed sharp closure of the sphincter, well marked in the first discharges in fig. 17, at other times an abrupt cessation with the first lessening of abdominal pressure. When Case 3 was instructed to attempt to micturate he responded by voluntarily increasing his abdominal pressure, and here the record of pressure in a balloon applied to the perineum shows by separate manometer a forcible bulge of the flaccid perineum downwards (fig. 31). The outflow commences gradually and lessens in volume immediately the straining is lessened, to cease abruptly a brief interval after the cessation of the straining movement.

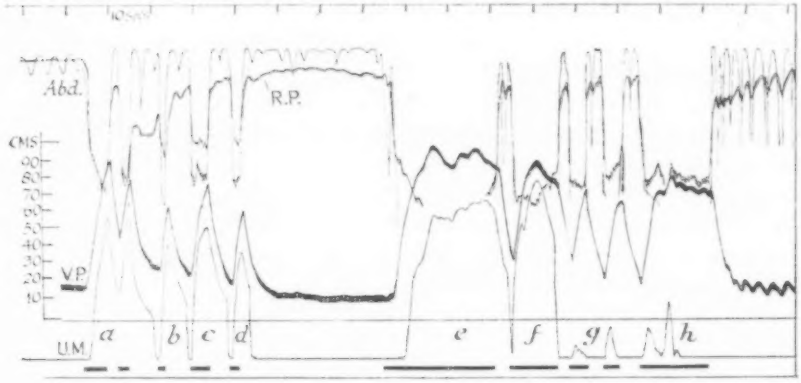

FIG. 17.—To show voluntary micturition by contraction of the abdomen and diaphragm ("straining") in Case 1. The duration of each such voluntary strain is indicated by the horizontal black lines at the bottom of the figure. In order to clarify the figure the records of vesical pressure and urethral discharge have been displaced vertically with due attention to time relationship. Reduced to $\frac{2}{3}$.

The delay in the fall of outflow pressure is related in all three cases to some delay in the fall of the vesical pressure, not so clearly seen in the records from Cases 1 and 3 as in some records from Case 2 (figs. 18 C and 32 B), and taking the form of a small late induced wave of vesical pressure. In all three cases a similar strain when the vesical pressure was registered by a more sensitive manometer and wider catheter was immediately followed by a brief induced wave of vesical pressure (as in fig. 14). The longer the duration of the strain the less obvious were both this subsequent induced wave and the delay of closure of the sphincter (fig. 32 E). There is evidence, therefore, that the delay in closure of the sphincter is directly related to the presence of vesical contraction in all three patients. A prolonged effort to pass urine by

straining succeeds in maintaining discharge only for a brief period, after which any slight relaxation of the effort is accompanied by a jerky closure of the sphincter (fig. 32 D), with renewed discharge on further effort. Eventually the discharge ceases in spite of continuation of the effort, and still far short of complete evacuation of the bladder. After a very brief rest further effort could secure renewal of discharge and the bladder could be completely emptied by means of a series of repetitions of straining (fig. 17).

Pressure upon the abdominal wall of any of these three patients succeeded in expressing fluid through the sphincter. The vesical pressure at which discharge commenced was constantly higher than that at which discharge commenced when the patient made a voluntary strain (e.g., in Case 2, 26 to 32 cm., and in Case 3, 48 to 75 cm.), but this difference is partly, if not wholly, dependent upon the manner the vesical pressure is passively increased. It is not possible, without risking damage to the viscera, to apply powerful manual pressure so rapidly as the wide piston movement of the diaphragm effects. The more rapidly pressure is passively applied, and the more jerky the pressure at its maximum, the more effective it is in securing discharge, and it is in these factors that manual compression of the abdomen fails to make complete imitation of voluntary strains (cf., *a*, *b*, with *c*, *d*, fig. 32 A). The discharge induced by manual compression is in every other way identical with that provoked by voluntary effort. The delayed closure is exactly comparable in form and extent (fig. 18 D at *f*). A brief pressure upon the abdomen did not alone suffice to provoke discharge in any of these patients, and likewise a cough did not cause any discharge from an inactive bladder.

It was noticeable in all three cases that the effect of abdominal pressure or of a strain by the patient was profoundly influenced by the state of the vesical pressure immediately preceding the induced pressure, whatever the volume of vesical contents. If the pressure had been low, a high passive increase is without effect in provoking discharge (figs. 32 A 16 F). With intermediate previous pressures discharge is more readily provoked by lesser effort (fig. 32 C), and when vesical contractions are in progress (figs. 16 E at *a*, 16 D at *d*), and especially if spontaneous discharge has just occurred (fig. 16 B at *c*), the slightest applied pressure opens the sphincter. Passive pressure thus used as a test of the resistance of the sphincter reveals that spontaneous detrusor contraction, both in the form of waves and in maintained tonic contraction, is accompanied by laxity of the sphincter. The degree of laxity of the sphincter is directly proportional to the degree of active vesical contraction, both

during actual discharge and during vesical contraction without discharge. When active detrusor contraction is slight or absent the sphincter is firmly contracted. We may apply this finding to the explanation of the delayed closure of the sphincter following passive pressure on the bladder. The small induced wave of vesical pressure, though in other circumstances not sufficient to be accompanied by discharge (as in fig. 16 F),

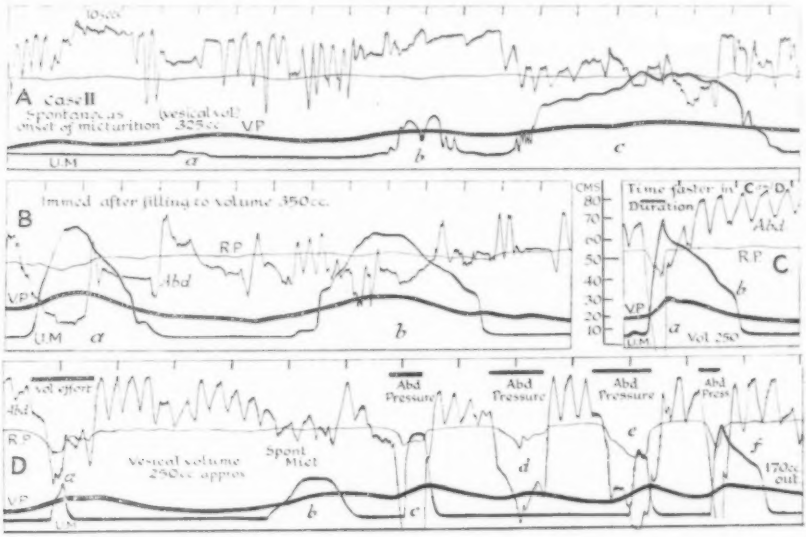

FIG. 18. *Case* 2.- The record A shows the gradual development of spontaneous micturition at constant volume in the absence of any extraneous stimulating factor. The even curve of rectal pressure excludes the respiratory arrhythmia from any direct relationship with the form of the micturition. In B is shown rhythmical discharge induced by distension at moderate rate. In C a voluntary strain at *a* induces discharge, and a continuation of the same piece of record in D contrasts the effect of passive pressure through the abdominal wall. The tension scale attached to C applies to the vesical pressure (V.P.) in all records. Reduced to $\frac{2}{3}$.

here combines with the declining remainder of the passive vesical pressure to maintain patency.

Attempts by these cases to obtain micturition by voluntary relaxation of the perineum, as is attained by the normal [15], were without influence upon vesical pressure. No vesical waves appeared and no relaxation of the sphincter or perineum occurred. An order to restrain micturition had no effect on detrusor tone, or on discharge when that occurred, and did not hasten the delayed closure of the sphincter. Only in Case 2 was there evidence of involvement of the upper lumbar nerve

roots in the lesion. Presumably, therefore, the hypogastric innervation in the two other cases was intact, but could not be activated by effort of will. It is possible that the difference in opening pressure between an active strain by the patient and a passive pressure upon the abdomen by an observer is related to some voluntary effect via the hypogastric nerves. Such an effect was not observed to occur alone, and in the absence of change in vesical contraction, or independent closing or opening of the sphincter produced by it, we prefer to regard the difference as a purely mechanical one.

Withdrawal of the catheter so that it lay some 10 to 12 cm. distal to the internal sphincter made no change in the form of discharge. We were unable to find any evidence of a functioning external sphincter in these cases. Efforts to "hold hard" produced either no withdrawal of the perineum, such as we have described in the normal subject [15], or sometimes only slight withdrawal directly related to a fall in intra-abdominal pressure, due to inspiration. The only effect upon the flow of discharging urine was that induced by the fall of pressure with the manœuvre and directly reflecting the fall in abdominal pressure. In none of these patients had plantar stimulation any effect on vesical pressure, sphincteric discharge or perineal posture, where the latter was recorded. The external sphincter shares the flaccid paralysis of the remainder of the perineum.

During spontaneous vesical activity the internal sphincter reacts by relaxations reciprocal with the intensity of contraction of the detrusor, and during a series of waves this is very striking (figs. 16, 18). Cases 1 and 2 may be considered as typifying the automatic micturition following complete sacral lesions, whether by affection of nerve roots or of the conus medullaris. The innervation of the bladder by means of the sympathetic nervous system, though capable of effecting contraction of the internal sphincter when stimulated directly [38], is not available for voluntary effects, just as reflex micturition cannot be served by it in the cat, as was shown by Stewart [51].

In Case 3 there was an improvement from the initial retention of urine, but analysis proves it to be largely a mechanical micturition. The detrusor here has regained some spontaneous activity in the form of reaction to distension, both sudden and gradual, and possesses feeble rhythmical activity. The internal sphincter, more lax than in the state of retention, allows straining to force it mechanically (fig. 31). There is a clinical history of the development of this laxity, which was contemporaneous with the change from retention to dribbling incontinence.

We have shown that laxity of the sphincter is related to the coincident active contraction of the detrusor in Cases 1 and 2, and in Case 3 we may relate it to the same process.

Six months after the time of the experiment in Case 3, voluntary effort was completely lacking, and apart from a rather more brisk reaction to distension and a slight sensation from catheterization, was identical with that here described. We have no doubt that the activity here described is devoid of central effects. The long interval during which this patient failed to establish automatic micturition calls for comment, and we feel that the inflammatory nature of this lesion and its probable extension to the autonomic plexuses hold the explanation of the failure of automatic micturition.

(2) *The Effect of Transverse Lesions of the Spinal Cord above the Sacral Segments.*

Three patients (Cases 4, 5 and 6) suffered from a variety of "active" clinical incontinence associated with reflex activity of isolated segments of the spinal cord. This incontinence occurred spontaneously in intervals of complete rest, in response to the gradual distension of the bladder by urine. The slightest movement of the patients, provided a flexor spasm was not invoked, often promoted micturition within three or four seconds, even if the bladder were only moderately distended. No micturition occurred with moderate flexor spasms (involving the abdomen in Cases 4 and 6), but *after the subsidence* of a severe flexor spasm or induced flexion, micturition tended to occur if the bladder were already distended. In Cases 4 and 5 a well-defined forceful automatic micturition was readily facilitated by the swabbing of the penis preparatory to catheterization. In all cases, including Case 5, in whom no reflex flexion was obtainable, clinical observation of the effect of a scratch to the sole of either foot revealed immediate complete suppression of micturition when that had been commenced by other means. After this sudden cessation of flow, discharge would rarely recommence, or only after an interval sufficient for the motor effects of the stimulus to subside. Cases 4 and 5 showed turgescence which subsided immediately micturition was elicited. We were not able to bring about erection by stimulation.

Our experiments succeeded in differentiating between two distinct closing mechanisms which we have reason to believe were the internal and external sphincter.

The internal sphincter.—When we had made observation of the

effects of distension of the bladder with both catheters recording vesical pressure, the two were very gradually withdrawn until the manometer of the larger catheter abruptly ceased to show the respiratory fluctuations which characterize vesical pressure. If the outlet tap of the apparatus connected to this catheter were opened partially, no discharge of the fluid occurred, though its outlet lay below the level of the symphysis pubis. The catheters are then held rigidly at this level and vesical contractions are induced. The resulting discharge from the sphincter is poorly defined in both onset and cessation (Case 4, fig. 33, Plate XV, and Case 5, fig. 34, Plate XVI). The vesical pressure shows the origin of the disturbance in one of the "maximal" isolated contractions resulting from distension in these two patients. The pressure at which opening and closure of the sphincters occurs is low. Indeed it is often difficult to be sure that the urethral catheter is out of the bladder. When the micturition is provoked by massage of the abdomen, as in fig. 33, the sphincter is at first unaffected by the passive increase of pressure, but later allows the passage of a few drops between each increase, and swings open only as massage ceases and vesical contraction is in progress. Steady increase of passive pressure on the abdomen secured discharge only if active vesical contraction were in process. The pressure in the posterior urethra required to force the sphincter in the absence of active vesical contraction is moderate (35 cm.). Plantar stimulation (fig. 33) influences the discharge only in the slight fluctuations of pressure which, through the vesical pressure, reflect the abdominal movement which such stimulation induces. Records from Case 6, fig. 35, reveal the same characteristics, although here the vesical contraction is of very low amplitude, and the resulting discharge is poorly defined.

Strong passive pressure on the abdomen may cause a drop of fluid to pass the sphincter at the maximum of pressure, but does not secure wide opening or sustained discharge unless the rise of vesical pressure is sustained after the release of the pressure. The sphincter opens spontaneously only in the presence of a wave of vesical contraction, and its opening and closure are related to the ascent and decline of such vesical waves. It showed no rhythmical or other activity unrelated to contraction of the detrusor. Sharp closure at high vesical pressures such as has been observed in the normal internal sphincter [15] has not been seen, though smaller sharp closure occasionally occurs, as in the last response in fig. 33.

In Case 6 the internal sphincter was much more readily forced by

passive pressure than in Cases 4 and 5, and the appearance of a further few drops after an interval reveals the presence of secondary contraction (fig. 36). When the volume was increased gradually the internal sphincter dribbled periodically in small amounts (1 to 10 c.c.) when 400 c.c. or more had entered the bladder.

The external sphincter.—If the urethral catheter is moved further distally for some 2 to 5 cm. the discharge during micturition is interrupted by plantar stimulation or involuntary flexor spasms. The characteristics of the discharge are altered; it commences abruptly (Case 4, fig. 38, Case 5, fig. 19), is liable to sudden lapses, complete and incomplete, and terminates in a sudden sharp fall. The pressure of the

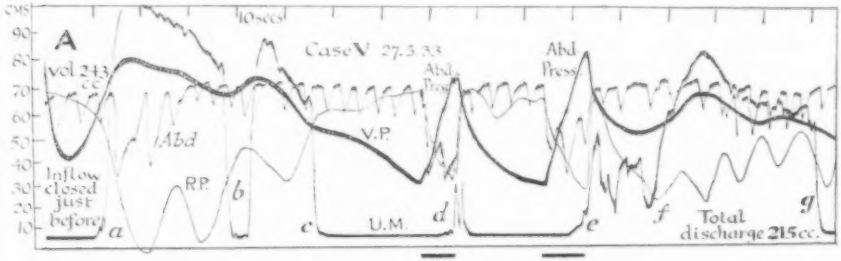

FIG. 19. *Case 5.*—To show spontaneous micturition induced by continuous inflow of fluid into the bladder, which ceases just as the figure begins. The spontaneous discharge past both sphincters is indicatsd by the urethral manometer U.M. After its cessation at *c* abdominal pressures (durations indicated by horizontal black lines) cause slight discharge at *d* and *e*, and eventually renew spontaneous discharge from *f* to *g*. The tension scale calibrates the vesical pressure (V.P.). Reduced to ½.

fully developed discharge varies with the vesical pressure. The pressure at which discharge commences and terminates is much higher than in the case of the internal sphincter alone. The opening and closure are frequently stammering in nature. The sudden lapses in discharge often correspond with sharp movements in the perineum, each of which leaves a small but rapid flicker in the perineal record (*a* in fig. 38, and *a*, *b*, *c*, *g*, and *h*, in fig. 39). These movements are due to perineal contractions, each corresponding to an involuntary flexor spasm. Their amplitude varied widely, and sudden complete cessation of vesical discharge was occasionally initiated by such a contraction.

In Cases 4 and 5 discharge occurred only with large maximal responses. If, however, these were prolonged and showed smaller superimposed waves, discharge ceased abruptly during the troughs of some waves (fig. 19 at *b*, and fig. 39 at *f*). The pressure of discharge

mirrors the vesical pressure, showing only the direct transmission of the latter through the widely open sphincter.

Micturition in Case 5 was invariably accompanied by rhythmical contractions of the rectum (figs. 19, 34, 44) and these were also often seen in Case 4, though here the rhythm was not usually so apparent (figs. 33, 38).

The external sphincter in Case 6 allowed discharge with smaller vesical contractions and these discharges were of the same small dribbling character as through the internal sphincter. A sudden closure rarely occurred (fig. 37). Spontaneous diphasic interruptions were frequent. The external sphincter in Case 6 could be readily forced by passive pressure on the bladder.

Stimulation of the sole of the foot provokes an abrupt cessation of discharge (figs. 41, 42, 43 and 44). The latency following stimulation is very brief (within one-tenth of a second after a single prick). The pressure of discharge shows a slight upward jerk followed by steep decline, and accompanying this diphasic movement there occurs a sudden jerky movement of the abdomen, a rise in the rectal pressure, and a downward bulge of the perineum by the increased abdominal pressure (figs. 39, 40, 41, 42). The vesical pressure shows a small steep rise followed by an equally steep decline (figs. 41 *b*, 40 *a*, and 45 *a*). After an interval of complete closure the sphincter opens abruptly, with often a small downward initial flicker. This diphasic type of closure of the external sphincter has been observed in normal men [15], and is interpreted as the result of the sudden powerful contraction of a muscle over a small length of the urethra to express any fluid it contains, and thus produces the initial upward jerk. The brief latency of the cessation of outflow can be explained only by contraction of striped muscle.

In Case 5 this type of closure was also present, but was frequently incomplete after a single prick, though it could be made complete by a more prolonged stimulus such as a scratch of the sole (fig. 44) or a series of pricks in rapid succession. The same phenomenon was observed in Case 6 (fig. 43). The effect in all patients outlasted a single stimulus by a very brief interval only.

Pricks to the glans penis also caused abrupt diphasic closure of the external sphincter (figs. 45, 52, 53 and 54); repetition (summation) was necessary to achieve prolonged arrest of discharge. If no discharge were occurring the sphincter did not open in response to such a stimulus, even if vesical contraction were in progress (figs. 40 *d* and 42 *c*), but a small flicker in the manometer shows that the contraction in the

perineum disturbed the urethral catheter opening. The external sphincter was at this time closed, as a test subsequently described will demonstrate.

The small steep ascent of vesical pressure accompanying sudden closure of the external sphincter is more obvious if the previous outflow has been voluminous and vesical pressure rising (fig. 40 *a* and fig. 45 *a*). This is referable to the sudden jar to the shortening detrusor caused by abrupt arrest of the escape of the contents. The contracting detrusor abruptly meets resistance. If the outflow is constricted so that little fluid passes and micturition is prolonged, the increase is less sudden and smaller (fig. 39 *d* and *e*). This has also been observed in the normal bladder [15]. The sudden "jar" does not appear to stimulate further contraction of the detrusor, and the pressure commences thereafter to decline, often very rapidly. If a brief stimulus falls early in a powerful micturition there is immediate resumption of discharge after cessation of the stimulus. Reflex closure of the sphincter is more brief if induced before or during the initial peak of the vesical contraction, but if it occurs later it frequently is followed by decline of the micturition (fig. 40). If the closure of the sphincter is prolonged and the vesical contraction has fallen low in the interval the renewal of discharge depends on the height of vesical pressure (cf. figs. 40 *c*, and 41 *c*).

A rapid pressure to the abdomen during discharge of urine causes a sudden rapid increase of output pressure (by direct transmission) followed by abrupt lessening of discharge for a brief interval. The sudden tension on the contents of the urethra appears to stimulate closure of the external sphincter. As with the internal sphincter alone, expression of fluid by passive pressure on the abdomen is difficult when no vesical contraction is present, and easier the greater the degree of existing vesical contraction. Rhythmical pressure (massage) was the most efficient method of inducing micturition; it did so by exciting active vesical contraction (figs. 19, 38, 41, 44 and 45).

In order to determine the manner of closure of each sphincter, and their relationship in time when both were allowed to function, we withdrew the catheters so that the proximal narrow catheter lay between the two sphincters and the wider catheter lay distal to the external sphincter. Both catheter systems are allowed to leak so that cessation as well as the onset of discharge is shown. When micturition is promoted by abdominal massage the manometer of the proximal catheter records a gradual rise of pressure for some seconds before the external sphincter swings suddenly open (fig. 47 at *a*). The external sphincter closes more

abruptly and earlier than the internal sphincter at the termination of discharge. During discharge thus caused, plantar stimulation (fig. 47 at *b*) causes the usual diphasic jerk and complete closure of the external sphincter. The catheter in the posterior urethra shows a rise of pressure and then a gradual decline, but does not close until vesical pressure has reached a low level. An involuntary spasm of flexion has the same effect. In recovery from brief closure the internal sphincter opens before the external if vesical contraction is maintained. Fluid introduced into the posterior urethra by means of the proximal catheter failed to pass the external sphincter or provoke its relaxation, but flowed readily back into the bladder when the reservoir pressure was greater than some 35 cm. water (Cases 4 and 5). The external sphincter therefore presents a maintained tonic contraction, whether there was spasticity below the level of the transverse lesion (Case 4) or when the tone of all other voluntary musculature was diminished or absent, as in Case 5. Vesical contraction is the only effective stimulus for its relaxation, and it occurs secondarily to that of the internal sphincter. Once relaxed in the course of a micturition it could be immediately and forcefully closed by peripheral stimulation. Spontaneously occurring flexor spasms were accompanied by variable degrees of partial or complete closure of the sphincter. The irregular jerkings of perineum and sphincter due to "flexor spasms" may at times cause rapid stammering, as in figs. 38 *a* and 39 *c*. A sudden increase of vesical pressure, such as that which accompanies sudden abdominal pressure, during micturition may cause closure of the sphincter, but vesical pressure may be unaltered by a weak flexor spasm or reflex flexion which nevertheless secures complete and lasting closure of the sphincter; closure is therefore a direct effect. The internal sphincter may be readily forced by passive increase of vesical pressure. Its lax condition reciprocates with the heightened activity of the detrusor. The resistance to catheterization of Cases 4 and 5 is due to the maintained activity of the external sphincter, the reflex control of which will be discussed below. In Case 6 both sphincters were less tonic, but although the limb reflexes were well developed, movements of the perineum and anal sphincter were weak.

The apparently invariable reciprocal relationship between the detrusor and internal sphincter suggests a fixed anatomical relationship such as would be provided by bifurcation of axis cylinders, but this lacks anatomical confirmation. The hypothesis of Heiss [28] that a sling of muscle from the trigone functions mechanically as an internal sphincter fails to account for the difference between the state of acute retention

and such a state as is presented by Case 3. The control of the external sphincter must certainly be mediated by the sacral segments via the pudic nerves, and an adequate mechanism for its relaxation during micturition is provided by the fifth reflex of Barrington [3]. Our records indicate that contraction of the bladder is the essential stimulus rather than increased pressure which was suggested by Barrington.

Not only did the external sphincter not relax when fluid was introduced into the posterior urethra in Cases 4 and 5, but no change in vesical pressure, as recorded by the second catheter, occurred. Even when some fluid is forced from the bladder past both sphincters by passive pressure upon the abdomen (fig. 19 at *c*) subsequent micturition awaits the development of vesical contraction, which was then identical with that set up by a similar pressure without the passage of fluid. The presence of fluid or tension in the posterior urethra appears therefore to have no appreciable effect on the bladder, and our findings fully confirm those of Frankl-Hochwart and Zuckerkandl [18] in the normal bladder. The activity of reflexes arising in the human urethra and facilitating vesical contraction or urethral relaxation is either extremely feeble or non-existent.

V.—The Disturbance of Sensation.

The descriptions of the sensations experienced by these patients during distension of the bladder and during micturition were extremely diverse, but could be classified into two groups. A common sensation in all patients, except Case 6, was a sense of fullness of the abdomen when the bladder contained a high volume, and appeared directly referable to a slight respiratory discomfort. It was not related to any particular region by the patient, and appears to be referable only to increase of abdominal capacity and therefore not related directly to the bladder. The other sensations are more particular and will need more consideration. Of the patients with cauda equina lesions, Case 3 presented the most discrete sacral lesion, although the inflammatory nature of his lesion does not allow absolute finality of deduction. He had no sensation from catheterization. During gradual distension he complained of fullness of the abdomen, indefinitely localized, as a volume of 150 c.c. was reached. At a volume of 200 c.c. the sensation developed gradually into painful discomfort which was felt periodically, and its lack of direct relationship to vesical contraction is instanced by its sudden appearance some seconds after a few faint waves had subsided. Filling the bladder from 200 c.c. to 300 c.c. induced pain vaguely referred

to the lower abdomen, which became continuons as the volume of 300 c.c. was reached.

Case 2, with clinical evidence of destruction of the cauda equina up to the level of the lower borders of the left fifth and right fourth lumbar segments and recovering function in the lumbar roots, first felt some fullness related to the abdomen at a volume of 335 c.c. An unpleasant sensation, referred vaguely to the left groin, commenced at a volume of 450 c.c. and became rapidly painful when filling was carried further. It was distinctly periodic. In the second experiment he complained of this periodic pain at a volume of 370 c.c., and referred it as before to the left groin. By signalling the periods during which it was felt we found that the pain frequently commenced with the onset of a spontaneous wave of vesical pressure and outlasted several subsequent waves. At other times it was more brief than one wave (fig. 10 E). It would disappear often without any corresponding change of pressure. In a third experiment fullness of the abdomen was first complained of at a volume of 275 c.c. There was no sensation with waves of contraction below this volume (fig. 10). The slightly earlier onset of the sensation of distension in the last experiment might possibly be identified with some recovery of hypogastric innervation. The fullness of the abdomen carried with it no desire to micturate. The unpleasant or painful sensation was also not comparable with normal desire to micturate, for each phase was of extremely sudden onset and intensely unpleasant and was a desire to micturate only in that he would feel a most powerful desire to strain with his abdomen and thus rid himself of it.

Case 1 complained of a slight momentary unpleasant sensation referred to the penis during the first of spontaneous waves of vesical pressure which appeared at a volume of 100 c.c. and again at 150 c.c. (fig. 8). At 160 c.c. he felt a "pumping," throbbing sensation in the upper parts of both thighs, of sudden onset, preceding an outburst of waves of vesical contraction (fig. 8 E). This was repeated with more unpleasant tingling referred to the penis, as further spontaneous waves appeared (fig. 8 F), and became more prolonged as the series of waves lengthened (fig. 9 A). During a later filling a sensation of discomfort referred to the penis, which was completely insensitive, and the thighs, was associated with a sudden momentary desire to pass water, which was extremely unpleasant. This was renewed during a rapid refilling from 100 c.c. to 150 c.c. (fig. 9 B). He once had a sensation of desire to pass flatus and a large rectal contraction was recorded after about six

seconds. A similar occurrence is seen in fig. 8 B. This patient also was not conscious of catheterization.

Both Case 1 and Case 2 at first stated that they possessed a sensation of desire to micturate, but close questioning elicited that this sensation was unpleasant or even painful and its rapid development induced them to strain voluntarily. Case 2 stated that he could postpone micturition, but this on close questioning was found to mean that he could tolerate the sensation longer before making a strain to commence micturition. In all three cases a sense of "fullness of the abdomen" formed a very definite part of the sensation during an experiment, but it was probably owing to the binder which was necessary to record abdominal movement.

The three cases with spinal transection experienced no sensation of micturition, with the exception that once in Case 5 some general abdominal fullness was complained of at a vesical volume of 200 c.c. When the binder for the abdominal balloon was readjusted he had no further sensation from distension up to over 300 c.c. During one experiment the occurrence of a large isolated wave of contraction on the recto-colonic balloon was preceded by a sensation of some "slight feeling" in the left lateral abdomen.

The lowest cutaneous sensation in Case 4 was from the right tenth dorsal segment and the left eleventh dorsal segment, and in Case 6 the third dorsal segment. In Case 5 all sensation was absent below the right first lumbar segment and tenth dorsal segment on the left side (fig. 26). Case 4 therefore should possess integrity of that portion of the hypogastric innervation of the bladder which is derived from the right eleventh dorsal segment, and Case 5 from all the hypogastric outflow on the right side. Dr. Carmichael informs us that the right lower limb in Case 5 sweated when the room temperature was raised and this is evidence that the hypogastric (sympathetic) innervation was not impaired on that side. There was no sweating on the left side.

Not only, therefore, may an intact hypogastric nerve give no sensation from the bladder, but the only points in common between the sensations perceived by Cases 1, 2 and 3, and that of normal desire for micturition and of distension, is association with powerful distension and vesical contractions. Their threshold is lower than for sensation in the normal bladder [15]. We agree with earlier writers [32, 2, 18] that normal sensation of the desire to micturate ("Harndrang") is not a function of sensory fibres conveyed by the hypogastric nerves.

The sensations in our cases referable to the hypogastric nerves are certainly provoked by vesical contraction, as Genouville [19] noted of

vesical sensation in general. We have found [15] that vesical sensation in the normal bladder may arise without vesical contraction though intensified by such contraction.

VI.—The Relationship between Automatic and Reflex Vesical Function.

(1) *Automatic Micturition resulting from Lesions of the Cauda Equina.*

We have described above the spontaneous automatic micturition we have found following lesion of the sacral roots of the cauda equina. Though our cases are few and the lesions unverified, the clinical states closely adhere to those described by other writers following lesions limited to the conus medullaris and verified at autopsy [41, 2]. This automatism may be identified with that observed in animals after destruction of the lumbo-sacral segments of the spinal cord [22, 41] or degenerative section of the nerves to the vesical plexus [14, 16].

The presence of the hypogastric innervation in connection with the intact portion of the spinal cord lends no voluntary control to vesical function, and, indeed, apart from often conveying sensory fibres it appears to be negligible as a functional entity both in animals and man. That automatic micturition is in any way mediated by it is unlikely, for in animals Elliott [16] and Dennig [14] found complete section of both hypogastric nerves neither to affect the appearance of the condition nor to cause change when the condition had developed. The excisions of spinal cord by Goltz and Ewald [22] and Müller [41] included the segments of origin of these nerves.

In each of our cases of cauda equina lesion the detrusor musculature possesses rhythmical activity even where automatic micturition is limited only to dribbling, as in Case 3. Increase of tension is the adequate stimulus for the appearance of this contractility. It is perhaps conceivable that spontaneous waves appear in continuous series which are merely thrown into prominence by increasing tension on the muscle fibre, but we have also demonstrated that the bladder reacts to sudden increase of tension by a secondary wave of contraction. Such stimulation of vesical contraction appears necessarily to imply a capacity of the muscle fibre to respond to stretch. While a purely local muscular effect for this phasic stretch reaction may not be completely denied, the regular waves of contraction during distension suggest a co-ordination of the contractile process in each fibre taking part. Such synchronizing of

spontaneous contractile waves in the whole organ necessitates nervous correlation of some kind. The same conclusion was reached by Elliott [16].

Regular waves of contraction are observable in the completely excised bladder when sufficient tension is imposed (Sherrington [47], Stewart [53]), but these are abolished by careful dissection of the minute mural ganglia (Elliott [16]). The presence of such waves is, however, insufficient alone to secure micturition, for they were observed by Sherrington [47] not to be affected immediately following section of the thoracic spinal cord in the monkey, when the process of micturition is profoundly shocked, and Barrington has shown [5] that in the cat there is no resistance to distension at this time.

Case 3, in whom discrete automatic micturitions did not develop differed from Cases 1 and 2 in that no wave compounds occurred. Though discharge through the sphincters occurred with some small waves in Cases 1 and 2 (e.g., in figs. 16 and 18), the waves are here larger and of longer duration than the unit small wave evoked by sudden distension. There is some evidence, therefore, that for micturition to occur not only must the spontaneous "beating" of the discharge of the vesical plexus embrace sufficient vesical muscle, i.e., involve approximately the whole detrusor, but also that two or more such waves must sum their effect by close approximation (temporal summation). The relaxation of the sphincter appears in records in simple inverse relationship with the contractile activity of the detrusor, so that as spontaneous waves become larger and longer there is greater and more prolonged relaxation of the internal sphincter. The fusions of large waves of vesical contraction into larger complexes is apparent in such records as fig. 18 A. Periodic automatic micturition is conditioned by the capacity of the spontaneous rhythm evoked by stretch of the detrusor to accelerate sufficiently to convert the muscular contraction into a periodic "motor tetanus." This process necessarily implies a correlation of the spontaneous "beating" of the neurones of the vesical plexus, and this in turn requires correlating neurones which dominate large numbers, if not all, of the scattered ganglia. The exact correspondence, the timing of these changes and the periodic relaxations of the sphincter are further strong evidence that extensive nervous correlation is active. There are, unfortunately, no available histological data on the existence of such correlating neurones in these ganglia, the complexity of which has defied histological analysis.

When the spontaneous waves are still single, as in Case 3, the

corresponding relaxation of the sphincter is reflected in a more continuous laxity, and consequent dribbling, which accompanies the tonic, more regularly maintained, resistance to the higher grades of distension. Periodicity is a more correlated development of this low-grade automatic micturition.

The full explanation of the stimulation of contraction by increase of tension awaits closer experimental investigation. To call it "reflex" appears premature, for if neither the pelvic nor the hypogastric nerves are essential for its performance there is no known remaining afferent neurone related to that collection of small ganglia which forms the vesical plexus. That the mechanism is essentially neural is certain from its affection by spinal shock. It may be recalled that Langley [35, 36] omitted the enteric plexuses from his conception of the sympathetic system as a purely efferent system and allowed in them a measure of true autonomy. Our findings entirely support the contention of Müller [41] that the vesical plexus also possesses a certain degree of autonomy. Although in our cases the hypogastric outflow was intact, the corresponding spontaneous micturition in dogs and cats with degenerative section of all nerves to the bladder renders insufficient any mechanism based upon axon reflexes in the inferior mesenteric ganglia or vesical plexus, and requires the presence of afferent neurones with cell body situated in the peripheral plexus, and there completing "reflex" circuits.

The smallness of the bladder in some cases is of especial interest and is apparently a constant accompaniment of such lesions in animals (Goltz and Ewald [22] and others), and is accompanied by great thickness and hypertrophy of the vesical wall, described in the human bladder by Lhermitte [39]. In Cases 1 and 3 there is evidence that the bladder will not tolerate much larger volumes than 300 c.c. and the steep curve of emptying, which is a fairly reliable index of the purely elastic reaction of the bladder without tonic contraction, reveals that small volume is related to structural change in the detrusor (figs. 1, 2 and 4). It appears likely that it is the result of a mechanical effect such as obtains for contracture in skeletal muscle. In the normal bladder involuntary reaction to increasing volume is continually subject to procrastination; the average vesical volume is more ample [15]. The fully developed automatic bladder of cauda equina lesions is never subjected to wide distension and the detrusor undergoes contracture to permanent smallness. The condition has been observed in the bladder of the cat after nerve section (16) and also after spinal transection [3].

(2) *Automatic Micturition resulting from Complete Transection of the Spinal Cord.*

When the nervous lesion isolates not only the bladder and vesical plexus but also a portion of spinal cord including the sacral segments, automatic micturition presents some striking additional characteristics both in reaction to distension and to external stimuli. Spontaneous single waves are still present, but are dominated by phases of explosive maximal contraction of compound nature which also shows a tendency to repetition in slow rhythmical series. These large contractions are also stimulated by increasing distension. They show evidence of compounding of smaller waves, and express, when fully developed, a maximal correlation of summation of muscle-fibre contraction. They are in fact tetanic contractions and must result from rapid repetitive discharge of nerve impulses in volleys. They are accompanied by concurrent prolonged and complete relaxations of the internal sphincter. Arguing from the invariable reciprocal relationship between detrusor and internal sphincter, these relaxations of the internal sphincter may be interpreted as the direct inhibitory result of the same discharge which affects the detrusor.

The general resistance to distension is heightened, forming a tonic background and steeply ascending filling curve which adapts readily to imposed volume. This process of heightened tonic resistance is paralleled by a coincident slackness of the internal sphincter, which we would explain as the result of a fixed simple reciprocal relationship between the two, evident in tonic as in phasic contractions.

The addition of segmental spinal pathways to the nervous mechanism of the vesical plexus endows the peripheral mechanism of reaction to distension with pathways for more extensive correlation. The afferent channels provide for greater efficiency of the tension receptors in the detrusor, the motoneurones allow closer collative activity of the neurones of the vesical plexus. The reaction to sudden momentary tension on the vesical wall is much larger than in the bladder following cauda equina lesions, though the latency of response is not materially altered (cf. figs. 14 and 15). One such sudden stretch is, however, in our experiments alone insufficient to provoke a "maximal contraction" which appears to require a summation of active vesical contraction before it occurs. An equivalent summation of the effects of repeated light stretches, or such brief changes of abdominal pressure as are induced by a cough, deep breath or movement of the patient, can excite maximal

contractions, but all require a certain amount of previous distension in addition. Volume is only significant when considered in relation to time, owing to the process of adaptation. The stimulus may be expressed as increment of stretch, and is exactly comparable to that underlying the postural reflexes of the limb muscles.

All these effects are, however, present in the bladder of cauda equina lesions. The characteristic feature of the vesical response which denotes the activity of spinal reflexes is the further process of the "maximal contraction," an explosive response which has a certain latency for elicitation and requires the pre-existence of active vesical contraction. The stretch effects related to the vesical plexus summate, but the summation subsides with cessation of stimulus. The phenomenon endowed by reflexly active spinal segments is that at a certain stage of summation active contraction becomes self-stimulating; the explosiveness of the reaction evidences autogenicity. We see in this process the effect of a fresh variety of afferent nerve ending which commences activity at a certain threshold of active contraction. The activity of this afferent system evokes a correlated discharge of the whole efferent mechanism. The discharge includes rectal activity, prominent in Case 5, less prominent in Case 4, and conspicuously rare in Cases 1, 2 and 3. There is, in addition, perineal movement and relaxation of the external sphincter, to complete the co-ordination characteristic of micturition of the spinal animal. Animal experiment provides ample evidence of the power possessed by the afferents in either pelvic nerve to excite reflex discharge through the other pelvic nerve [51].

No precise histological data on the relationship between preganglionic and peripheral neurones in the intricate vesical plexus is available. It may be compared, however, with the superior cervical ganglion where fibre and cell-counts reveal that each preganglionic fibre by repeated subdivision controls many ganglionic neurones [10] and so provides a basis for extensive correlation.

We have not had the opportunity of following the recovery of the reaction to distension from the initial depression of spinal shock, but it is clear from the work of Holmes [29] that, seen in full perspective, the reaction to distension makes a progressive development in parallel with all other spinal reflexes. Both phasic and tonic reactions of the bladder emerge in a gradual manner from the atony of spinal shock.

In its reaction to change of volume, therefore, this type of bladder differs profoundly from the bladder following cauda equina lesions. The difference is both quantitative and qualitative and is readily appreciable

in the regularity, large volume and force of discharge which form prominent clinical characteristics of this type of micturition. We fail to find any differentiation between this reaction to distension and that described by Barrington [3] as his "first reflex." We therefore cannot accept his pontine localization of the reflex mechanism concerned since we find the reaction present with isolated spinal segments, even the limited sacral segments as in Case 5.

The bladder innervated by the reflexly active spinal segments exhibits a further outstanding difference from the bladder of cauda equina lesions, namely a continued closure of the external sphincter, interrupted only by relaxations accompanying each summated vesical contraction. When once opened in this way the sphincter is immediately contracted by any flexion reflex. In Cases 4 and 6 brief scratching of the sole of the foot elicits reflex flexion of the ipsilateral limb, a movement which is accompanied by a contraction of the lower abdominal wall and of the perineum. The immediate change of intra-abdominal pressure brought about by these movements is reflected in a concurrent change in vesical pressure well shown in fig. 46 where discharge of fluid was not allowed and the pressure was therefore uncomplicated by cessation of outflow. The brief latency of these initial changes in vesical pressure, less than one-tenth of a second, following the onset of abdominal and perineal movement, and their rapid decline, exclude their origin from vesical contraction. The latency and form of the delayed response both closely resemble that of the response induced by brief increase of tension. We have attempted to exclude the incidental change of abdominal pressure as a cause of the contraction following plantar stimulation. Flexion of the limb and contraction of the abdominal wall and pelvic diaphragm is abrupt and jerky and lasts at least some seconds. Reduction of strength of stimulus does not succeed in abolishing the induced change in intra-abdominal pressure without also losing effect in evoking vesical contraction. Involuntary flexor spasms, or flexion occurring as a result of contact stimuli, are alike provocative of vesical contraction at times, as in fig. 46 *a*, but then are accompanied by a great deal of abdominal and perineal movement. Plantar stimulation at a time when micturition is not occurring and vesical content is small or moderate (fig. 40 *d*) sets up a wave of secondary contraction without micturition. When micturition is occurring plantar stimulation not only evokes abrupt cessation of outflow, but also, when the immediate pressure change of outflow stoppage has passed, may leave a declining vesical pressure and ultimate cessation of micturition, especially if the stimulus be long

continued (fig. 42, *c*), though reopening of the external sphincter occurs (figs. 40 *b*, 41 *c*). Early in a large response a brief plantar stimulation does not cause abolition. All these effects may readily be observed in the urinary outflow of such patients without any catheters or recording instruments, and are not alone evoked by stimulation of the sole, but from any part of the area from which reflex flexion can be elicited. It is necessary to conclude, therefore, that a stimulus sufficient to evoke a flexion reflex secures complete inhibition of micturition during the reflex flexion, but has a much weaker after-effect. This sudden cessation of micturition without doubt may be identified with its reflex inhibition in the spinal animal by "strong cutaneous stimuli" [48].

Head and Riddoch [27] described a rise of vesical pressure accompanying the flexion reflex, but it is noteworthy that although this "mass reflex" was present, discharge of urine through the urethra occurred in one instance only. Their patients possessed fully developed automatic micturition which regularly secured complete discharge per urethram. The lack of actual discharge of urine through the sphincter during the "mass reflex" was explained by the early return of tone to the sphincter mechanism, but in all our own cases added contraction of the external sphincter is effectively preventing actual micturition.

The induction of vesical contraction by a flexion reflex would appear to have some explanation as an indirect effect of the changes of intra-abdominal pressure necessarily also induced. The changes of abdominal pressure are jerky and multiple after even a single prick to the sole, allowing summation of multiple pressures on the bladder. The movements are sufficiently powerful to bulge the perineum (fig. 46 *a*, *b* and *c*).

Cases 5 and 6 were of particular interest in relation to the question of the facilitation of micturition by the flexion reflex. In Case 6 the flexion reflex existed in full development, both in area from which it could be elicited, in lowness of threshold, and in powerful motor effect. Whatever part of its afferent area was subjected to stimulation, the detrusor, lacking only in briskness of stretch response, failed to contract (fig. 50). The external sphincter was immediately contracted by these stimuli although the increase of abdominal pressure at times forced it (fig. 51). Stimulation of the glans penis also failed to set up vesical contraction in this patient (fig. 48), though it caused bilateral flexion of the lower limbs and more powerful closure of the sphincter than stimulation elsewhere (fig. 54). The lapse of one stimulus from a series of pricks reveals clearly the purely passive rise of vesical pressure which results

(fig. 49). Stimulation of the left side of the glans penis in this patient produced slightly more perineal movement than did pricking the right side, but was also without effect in evoking vesical contraction. The external sphincter showed well the summation of effect of a series of stimuli (figs. 43, 52 and 53). The degree of development of the flexion reflex appears therefore to have no direct relationship to its power of facilitation of micturition.

Case 5, owing to inactivity of the four lower lumbar segments of the spinal cord, though the sacral segments retained reflex activity, had no reflex flexion. The general reaction of this bladder to distension has been described above. Stimulation of the sole of the foot (fig. 44) or of the glans penis (fig. 45) evoked contraction of the external sphincter, and a degree of perineal movement which was much more powerful than the records indicate. There was a small vibration in

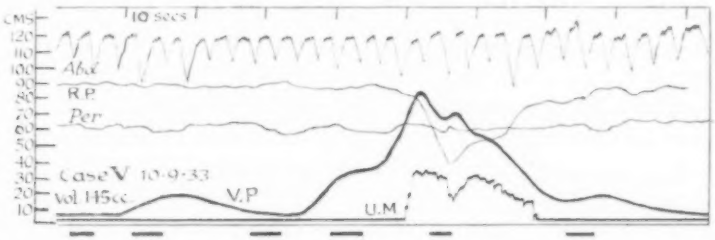

FIG. 20. *Case* 5.—To show the delay in rise of vesical pressure resulting from long slow scratches (duration indicated by horizontal lines at bottom of figure) to the sole of the left foot. The second and fourth scratches appear to impair the development of previous contraction. The catheter had not been completely withdrawn through the external sphincter so that the fifth scratch resulted only in partial monophasic interruption of the micturition which subsequently developed. Reduced to ½.

vesical pressure corresponding to movement of the perineum, but not comparable in degree to that in Case 4. Stimulation of the sole of the foot by single prick was seldom alone successful in eliciting vesical contraction, but repeated stimulation, or a scratch, was followed by a small vesical contraction (fig. 29 D at *c*, and fig. 58 at *a*). The contraction was identical in latency and form with that produced by brief tension (fig. 29 D). The response was larger with stronger stimuli such as a scratch, but was delayed until a certain latent interval after the scratch (figs. 20 and 58). During the development of a response further stimulation arrested further rise of pressure (fig. 20), but did not abolish the response unless the latter were very small. If recent filling had rendered the detrusor sufficiently active the effects of a series of scratches at

sufficiently short intervals summated so that a maximal response was eventually elicited by a single prick (fig. 58 *d*).

A single prick applied to the glans penis provoked a delayed vesical contraction (figs. 55 and 57) also identical with a stretch response, and when repeated in series more readily shortened its latency of development (fig. 55) and height of contraction (fig. 57). A rapid series of stimuli was more readily followed by a large maximal vesical contraction than stimuli elsewhere, but it also had some power of inhibiting contraction if strong (fig. 59). Reflex vesical contraction is most readily provoked by weak stimuli, and develops greater tension, when the stimulus is applied to the glans penis, which we regard as the "focus" of this effect just as the outer border of the foot is the "focus" for reflex flexion. Slight inward or outward movement of the catheter is also a strong stimulus of vesical contraction, and light swabbing of the penis or movement of the prepuce (fig. 56) provoked micturition after a brief interval. Lighter movement of the prepuce with care not to disturb the relation of the catheter to urethra did not evoke a response. The delay in appearance of these contractions following these cutaneous stimuli when applied in series is evidence of the dual effect produced by each stimulus. Powerful immediate inhibition suppresses even the excitatory effect of the same stimulus, and only at the end of the series is the excitatory effect declared. Similar "rebound" is frequently observed in limb reflexes. All these stimuli therefore possess some measure of excitatory effect on the detrusor, besides the immediate and more powerful inhibitory effect which accompanies contraction of the external sphincter. We do not think this excitatory effect is, in these circumstances, produced by the small associated perineal movement, for the bladder of this case required a greater degree of applied passive tension to excite contraction than in the more reflexly active case, and changes of abdominal pressure a little greater than those accompanying the reflex response were not successful in eliciting contraction.

Clinical examination of Case 5, however, revealed two features widely differing from the state necessitating the exhibition of the "mass reflex." Although stimulation of the glans penis or of the sole of the foot could bring about facilitation of vesical contraction there was no flexion reflex. Further, it was found that not only stimulation in these areas but also stimulation of the skin in any part corresponding to the innervation of the five sacral segments provoked a motor reflex response quite unlike reflex flexion. Immediately following a single stimulus both thighs slightly abducted, and rotated outwards more strongly, the

perineum as a whole was vigorously retracted with contraction of the external anal sphincter, and the great toe on each side was plantar-flexed. The other toes flexed slightly and were approximated. The response was constantly obtained and was increased by prolonged or repetitive stimulation. The motor effect was bilateral from stimulation on either side. The whole area of the sacral dermatomes could be mapped out by it. Stimulation of the lumbar dermatomes on either side, pinching the calf muscles, or eliciting ankle-jerks did not evoke the response. Contraction of the external sphincter of the bladder was as consistently elicited as closure of the external anal sphincter. Occasional slight turgor of the penis found after long intervals of absence of stimulation was abolished by any stimulus provoking micturition or provoking the response above described. No other movement in the paralysed musculature could be elicited. Dorsiflexion of ankle or great toe was not seen. The response appeared as easily elicited from the skin around the anus and from the narrow strip on the posterior aspect of the limb as from the glans penis.

Contraction of the external anal sphincter as a result of a stimulus to the skin around the anus ("anal reflex") has long been known as an early reflex response to emerge from spinal shock. This "anal reflex" is often the only sign of survival of lower spinal segments following a supraconal lesion. Oppenheim [42] has described how in one such case the anal reflex was elicited by stimulation of the sole of the foot as well as of the skin near the anus, although he does not describe any other motor response. We consider that the reflex response we have described in Case 5 is an extension of the "anal reflex." Its bilaterality, the abduction and external rotation of the thighs and the plantar-flexion of the great toes proclaims its complete independence of the flexion reflex, and the coitus reflex, with their contrary motor effects. We propose to call it "the sacral reflex."

The "sacral reflex" is accompanied by a twofold effect on the bladder. Accompanying the perineal and limb movement the external sphincter contracts and vesical contraction is momentarily inhibited. Following the direct motor effect vesical contraction is stimulated. The reflex facilitation of the detrusor has a focus at the juxta-meatal portion of the glans penis, while the inhibitory effect and contraction of skeletal muscle are as easily provoked from any part of the sacral cutaneous segments. Whatever the nature of the antagonism between these two components of the "sacral reflex" it is clear that the first is a true reflex facilitation of micturition.

The early emergence of the "anal reflex" from spinal shock strongly suggests that, in those cases where a "flexor plantar response" has been obtained in the first days of recovery from an acute transverse lesion of the spinal cord [30], the limb reflex constituting the sacral reflex has appeared. The subsequent substitution of dorsiflexion of the great toe when the sole of the foot is stimulated bespeaks the inhibition of the sacral reflex when the "prepotent" flexion reflex recovers. We have not had an opportunity of observing this transition, but in cases of various partial lesions and one other complete lesion, one of us has observed intermediate stages of domination of the sacral reflex by the flexion reflex.

As a result of investigation of Cases 5 and 6, therefore, we are led to the conclusion that true reflex facilitation of micturition by cutaneous stimuli does in fact exist. Its cutaneous area has a "focus" at the glans penis, and fades through the sacral segments. In Case 4 all stimulation was complicated by the flexion reflex, and we were unable with certainty to deny reflex facilitation from other areas because of the changes in abdominal pressure associated with it. It is certain, however, that inhibition of micturition was more powerful from all these other areas, and only with considerable degrees of existing detrusor excitability, for example, by recent rapid distension, could a flexion reflex evoke subsequent discharge. Stimulation of the glans penis in this patient, besides evoking reflex flexion, was potent in setting up vesical contraction. Attempts to separate the two components of the sacral "reflex" in Case 5 by variation of mode of stimulus, massage of the glans penis (fig. 56), &c., failed to make any such differentiation, though without doubt each has an adequate stimulus. Case 6 exhibited the type of micturition seen after cauda equina lesions, controlled by a reflexly active external sphincter.

Reflex micturition is characterized by explosive vesical contraction which, if our deductions as to origin from autogenetic stimulation be correct, may not be expected to exist long in incomplete form. Cutaneous facilitation in fact evoked such discharge only indirectly, in the same manner as sudden stretch or distension, and we did not find it possible to grade the size of contraction by the intensity or duration of cutaneous stimuli. At one period in one experiment in Case 5, it was found that cutaneous stimuli set up a small combined rectal and vesical disturbance after an interval (fig. 21). This was more readily provoked from the glans penis by one prick, than from the sole of the foot where a series of pricks was necessary. This disturbance did not appear to be graded, for stronger stimulation provoked only a maximal response, but the

associated delayed rectal contraction suggests that the afferent stimulation was reaching that efferent system concerned with the combined rectal and vesical maximal contraction so obvious in this patient. We did not find further opportunity to study the phenomenon, and can offer no explanation of the delay in reaction.

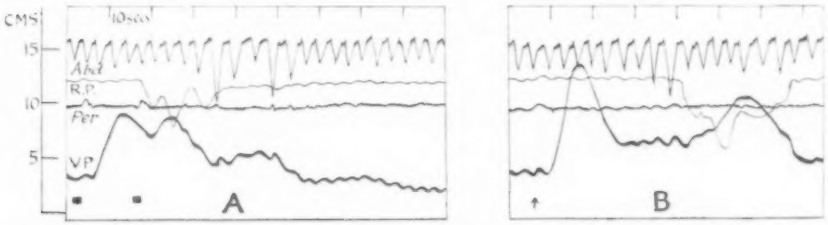

FIG. 21. *Case* 5. August 27, 1933.—Vesical volume constant, 100 c.c. In A the effect of two series of pricks to the outer border of sole of left foot induces vesical and rectal contraction. The duration of each series of pricks is represented accurately by a black square. In B is shown the vesical contraction stimulated by an accurately signalled prick (↑) in the neighbourhood of the urethral meatus. Reduced to ¼.

(3) *Reflex Co-ordination.*

To include the incongruous mixture of brisk, often bilateral, flexion with micturition and widespread sweating as one reflex, the "mass reflex" [27], belies the niceties of reflex co-ordination in every way apparent in the spinal animal. This incongruity in part disappears with our finding that contraction of the external sphincter is reflexly induced by stimulation of the skin surface, as well as some direct inhibition of vesical contractility. The latter is mixed with the directly stimulating effect of abdominal movement. The external sphincter provides an adequate security for the abolition of micturition during reflex flexion and other reflexes. The promotion of evacuation of urine through a catheter by the flexion reflex ("mass reflex") is nullified by contraction of the external sphincter. Patients with reflexly active spinal segments possess an automatic, and usually complete, periodic evacuation of urine which is the result of natural distension of the bladder, although the immediate stimulus was usually some abdominal movement.

We see no justification for the inclusion of micturition in a progressive abolition of "local sign" of reflexes such as that hypothesized for the "mass reflex" [27] and flexion reflex. Indeed, by the well-defined physiological notion of "local sign" (Sherrington [50]), meaning a functional adaptation of reflex movement according to locus of

afferent stimulation, the flexion reflex *gains* local sign in its fuller emergence from spinal shock, rather than loses it. When the afferent areas include the thigh there are specific differences in the reflex, according as its outer or inner side is stimulated. The scratch reflex likewise gains local sign with increase in cutaneous area. The flexion reflex from the first affects proximal joints as well as distal joints of the limb; its characteristic physiological feature is withdrawal of the limb as a whole.

The enlargement of the area from which the flexion reflex can be elicited in the process of its emergence from spinal shock has explanation in the progressive recovery of excitability of the motoneurones concerned, without change in the distribution of afferent effects. The reflex fully emerged from spinal shock appears to physiologists the more "normal" reflex, albeit enhanced in after-discharge.

In the normal human being, as in "spinal man," a contraction of the bladder is evoked by a cough, sigh, or other sudden change in abdominal pressure [15]. It here shows the characteristics of the response to momentary change of tension in the automatic bladder, and has the same time relations. This reaction to sudden tension may be regarded as the basal postural response of the organ, as the tendon-jerk of the postural reflex is of striped muscle.

A process of storage of fluid and a process of discharge of fluid may not at first sight appear compatible functions of the same mechanism. Our analysis indicates, however, that the degree of progressive increase of volume which the organ accommodates before discharge occurs is directly related to the intensity of automatic micturition, and is determined by the facility with which stretch of the detrusor can activate the discharge of the neurones provoking contraction. Adaptation to volume in these bladders is seen only as a consequence of cessation or slowing of distension, and reflects the degree of response during the previous distension. The ultimate reaction is inevitable if distension is *progressive*. The only "adaptation" which then occurs is the trough following a maximal fused contraction, and this in turn gives way to another such contraction if distension continues. If the volume is then kept constant, as in figs. 11 and 12, the reaction eventually subsides, only to be renewed with further increase in volume. Each such reaction represents a micturition, which is here only prevented by the occlusion of the catheter. It is thus not comparable to the "plastic tone" of skeletal muscle. In the normal human bladder, on the other hand, adaptation occurs with smaller contractions arising at intervals

during distension, and is interpreted as the result of inhibition arising from higher nervous levels [15]. The mechanism appears to be identical with that which has been described for rectal function in man [31].

The central locus of co-ordination of vesical activity lies within the small sacral segments of the conus medullaris. We have described the close interaction of automatic micturition, rectal contraction, reflex micturition, and reflex facilitation of micturition, when the functioning spinal segments are restricted to the sacral group. Even in this state micturition does not occur as an isolated nervous discharge but is closely bound in a complex reaction, and for this reason we have refrained from the use of the word "centre." The spinal reflexes use the efferent neurones at their command as a whole, and the activity of one set involves the coincident appropriate adjustment of others.

Micturition in reflexly active spinal man is, by reason of reflex inhibition, frequently incomplete. For that reason it is not uncommon to find considerable volumes of urine remaining in the bladder immediately after a micturition, even in Case 5 where the field for reflex inhibition was limited. Equally frequently Cases 4 and 5 secured complete evacuation of the bladder, and under conditions of experiment micturition was often complete. It has been argued [5] that the small amounts of residual urine often found in the decerebrate and spinal cat are evidence of inco-ordination of micturition. On the contrary, the incompleteness of reflex micturition in the spinal state, and probably also in the decerebrate state, offers evidence of perfected co-ordination and greater harmony between reflexes.

It becomes apparent, therefore, that *moderate* volumes of "residual urine," unless considered in conjunction with the circumstances of the preceding micturition and the details of other micturitions, are without value in estimating the state of micturition. The transition from complete depression of micturition due to spinal shock to recovery of automatic micturition, is by degrees of increasing maximum volume of discharge from decreasing volume of vesical contents. The reverse transition as a result of gradual reflex failure repeats the same stages, of which our Case 6 may be taken to represent an intermediate state. A more important clinical indication of the state of micturition is the volume of the greatest single micturition over a period of twenty-four hours. The volume of residual urine after *the most complete* micturition changes in inverse proportion, but only the considerable volumes of residual urine in states of almost complete failure of vesical function are, when considered alone, of significance.

Close comparison of the records of uninterrupted micturition and of vesical contraction without micturition, in Cases 4 and 5, reveals no element of difference from the records of normal man shown in our previous paper [15]. The salient effect of will in micturition in the normal subject is voluntary suppression, which led us to postulate an hypothesis of voluntary control entirely by inhibition. No feature of spinal micturition appears to us to be incompatible with this conception.

Barrington [4, 5], as a result of a long series of carefully conducted experiments in the cat, concluded that the contraction of the bladder resulting from distension was abolished by interference with a relatively small region of the pons or with descending tracts from that region. Since cats failed to recover from such a lesion he considered this region of the pons an essential link in the reflex reaction to distension (his "first reflex"). We have here demonstrated the full reflex reaction to distension as a purely sacral segmental reaction, and, by analysis, find it only a correlated reflex discharge based on the reaction which can be elicited from the autonomic plexus alone. There is abundant evidence that in spinal man, as in the spinal dog, a reaction to distension occurs as a spinal reflex. The experiments of Barrington, however, localize with great accuracy the region and connections whose injury is responsible for a depression of micturition immediately succeeding pontine or lower section. It is indeed remarkable that this region is identical in level with that responsible for "spinal shock," and we would emphasize the exact parallel which exists between the limb reflexes and the "reflex" reaction to vesical distension. The frequency of micturition of the decerebrate animal thus derives, in our view, explanation as an enhanced spinal reflex, and reflects that enhancement of the stretch reflexes of which decerebrate rigidity is the most obvious outward sign.

VII.—Reconstruction of the Development of Automatic Micturition.

The sudden onset of a complete lesion of the spinal cord at any level has long been known to be followed by a period of retention of urine. The detrusor musculature lies atonic and the internal sphincter, in inevitable reciprocal relationship, falls into uninterrupted closure. The external sphincter, in common with other voluntary musculature, lies flaccid and toneless. We may reconstruct from our own findings and from the deeper perspective of the findings of Holmes [29] the following outline of subsequent events concerning micturition.

As the initial shock passes the detrusor awakens to greater develop-

ment of reaction to stretch and rhythmical contractions become more prominent. The re-establishment of micturition awaits sufficient degree of contractile activity, especially of rhythmical activity of the detrusor. At first a degree of intensity of vesical contraction sufficient to reflect only some laxity of the internal sphincter is attained and micturition by passive increase of vesical pressure becomes possible. In more ample development the same local mechanism gains, by periodic fusion of waves of contraction, a deeper and more prolonged reciprocal relaxation of the internal sphincter so that periodic discharge commences. Automatic micturition of low grade is thus established as a function of the bladder and related pelvic plexus. Unrestrained by any other activity it functions frequently, although often anticipated by passive increase of vesical pressure by straining and other abdominal movement. As automatic micturition gains in efficiency so the vesical volume lessens and the detrusor may even show contracture.

Further co-ordination of the contractions of the detrusor requires the assistance of correlation from the sacral segments of the spinal cord (true reflex micturition) which brings also an association of rectal and vesical activity. The integrity of these sacral segments also allows the recovery of function in the striped musculature of the sacral segments, including the vesical sphincter. This sphincter regains a postural tonic contraction even when these other muscles lie flaccid and the summated detrusor contractions in reflex manner secure its relaxation for discharge. The external sphincter provides the means for rapid co-ordination of micturition with other spinal reflexes.

True reflex facilitation of micturition is confined to the effects of stimulation of the sacral cutaneous segments, and even here is in greater part negatived by the further development of the omnipotent, "prepotent" flexion reflex. In spinal man, as in the spinal animal, manifold under-currents of reflex activity are hidden beneath any purposive movement, for which inborn reflex co-ordination secures perfected outward expression.

The pelvic nerve and the pudic nerve together form the efferent pathway for reflex micturition. The hypogastric innervation is without significance and may be disregarded in this connection, and disturbance of sensation referable to it gives equivocal indication of the location of disturbance. Occasionally fibres of long extramedullary course conveying sensation from the bladder allow undoubted vesical sensation, notably the pain of extreme distension, to circumvent a lesion even in the lower dorsal region. Our cases are not consistent in this respect. The

distribution of afferent fibres to visceral organs in common with sympathetic fibres allows wide segmental divergence and variability. Normal sensation of desire for micturition ("Harndrang") is regularly abolished by limited sacral lesions, though some sensation, usually unpleasant or painful, of imminent micturition may be retained.

Stretch of the detrusor is the adequate stimulus for vesical contraction and its effect may be sampled by a brief passive pressure. With the development of a simple automatic reaction after lesions of the cauda equina, there is a small response to brief pressure. With the more active bladder of the isolated segments of the spinal cord the reaction occurs to lighter pressures and is more brisk, while heavier pressures may impair the reaction. By the criterion of heavy pressure slowly applied on the lower abdomen the vesical contents are more easily expressible after lesions of the cauda equina. The reaction of the bladder of the reflexly active spinal segments to brief transient pressures is such that movements of the patient, coughs or deep breaths, more frequently commence discharge than uninterrupted filling of the bladder which is alone effective practically only during sleep.

Summary of Conclusions.

(1) The registration of the pressure of the contents of the human bladder during its distension reveals the occurrence of contraction of the detrusor elicited by stretch of that musculature. The reaction is elicited only by increment of stretch, and at continuous stretch or by decrease of stretch, the reaction progressively declines. The volume of the contents of the bladder expresses the stimulus for this reaction only when related to the proportion most recently added.

(2) Increase of passive pressure on the bladder likewise evokes contraction of the detrusor. By means of brief transient passive pressures small twitch-like contractions of regular duration may be elicited, and these are related to the general reaction to continued stretch. Passive pressure on the bladder derives greater effect if alternating in intensity, by reason of the response to rapid acceleration of pressure.

(3) This reaction of the detrusor to stretch recovers progressively from the shock of sudden complete transverse lesions of the spinal cord or cauda equina. The mechanism of the reaction is related only to the vesical plexus and detrusor, and a peripheral reaction of reflex character must be postulated to account for it.

(4) This reaction of the bladder to stretch is found in an enhanced form when reflexly active spinal segments make full recovery from

spinal shock. The mechanism is probably still wholly related to the vesical plexus.

(5) The sacral spinal segments may set up discharges of the whole detrusor mechanism by a reflex for which the adequate stimulus appears to be a certain degree of active reaction to distension. This is true reflex micturition and its discharge may affect the rectal division of the pelvic plexus as well as the vesical plexus. The hypogastric nerves play no part in the efferent reflex mechanism, or in voluntary control.

(6) The efferent neurones which serve reflex micturition are subject to excitation by cutaneous stimuli from the sacral segments with a focus of effect at the urethral meatus. The effect is smaller from the first and second sacral segments, and it is doubtful if it may be obtained from the lumbar segments. This is reflex facilitation of micturition.

(7) From the sacral segments a reflex response, the "sacral reflex," which includes the anal reflex, exerts a transient inhibition upon the discharge of reflex micturition. The flexion reflex exerts a stronger and more lasting inhibition of reflex micturition. Neither appears to inhibit the activity of the peripheral response to stretch, so that the abdominal movement with the flexion reflex tends by its stimulating effect to oppose the later stage of inhibition of reflex micturition. With the effects of the "sacral reflex" merges reflex facilitation of micturition.

(8) The internal sphincter reflects a degree of contraction reciprocal to that of the detrusor at the time, and is not under separate control.

(9) The external sphincter is reflexly active where the sacral segments survive, and maintains a tonic contraction which is relaxed reflexly by a certain degree of active vesical contraction. By its contraction in the course of all reflexes other than reflex micturition it secures co-ordination between micturition and these other reflexes whatever the state of activity of the detrusor. The recovery of tone in this sphincter appears responsible for the onset of late resistance to catheterization in these patients.

(10) The reactions of the bladder mediated by the vesical plexus and sacral segments of the spinal cord differ from those of the normal bladder only in lack of appropriate restraint.

(11) We recognize three fundamental states of disturbance of micturition by complete spinal lesions. A depression of function with inactive detrusor and tonic internal sphincter is the transient immediate result of a sudden deprivation of innervation. The development of incontinence during straining movements and later spontaneous inter-

mittent micturition characterizes the isolated survival of the peripheral plexus. A more facile and complete development of automatic micturition, co-ordinated with defæcation and subjected to the interplay of spinal reflexes, reveals the reflex behaviour of the isolated sacral segments of the spinal cord.

APPENDIX.

Description of Cases.

Case 1.—*Complete bilateral lesion of 5th lumbar and all sacral roots of the cauda equina.*

G. S., aged 26, admitted January 5, 1933, under the care of Dr. Gordon Holmes.

History.—Mining accident, February 9, 1932, with immediate loss of the use of both lower limbs and loss of sensation below the groins. Subsequent retention of urine. Indwelling catheter for nine days, and since then "incontinence" of urine associated with ability to assist urination by straining. He remained unconscious of bowel movements, which he could not control. After four months there was gradual recovery of flexion at the hip-joint and of some extension of the knees.

Clinical state at time of experiment.—Some weakness of the lower abdominal wall was revealed by bulging on coughing; flexion, abduction and adduction at hip-joints and extension of knees of moderate power: extension of hips and flexion of knees very weak. No voluntary power in movement of toes or ankles. Fibrillation present in glutei, with some wasting of glutei, vasti and

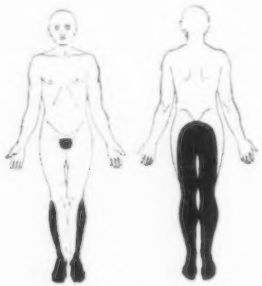

Fig. 22.

hamstrings on both sides; gross wasting of calf muscles and intrinsic muscles of feet. Reflexes: Lower abdominal reflexes diminished but equal, right knee-jerk present, left absent, both ankle-jerks absent. No plantar response. The anus was patulous.

Complete loss of sensation to all forms over an area corresponding to the

5th lumbar and all more caudal segments (fig. 22). X-ray of spine revealed fracture dislocation of body of 4th lumbar vertebra.

Micturition.—No actual knowledge of passage of urine apart from preceding abdominal sensation. He commenced micturition every fifteen minutes by straining down, and would strain until no further evacuation occurred. Micturition did not always result from straining. Urine would pass spontaneously if the straining process were not made sufficiently frequently, and he was unable to prevent its passage. For the duration of one strain the stream was relatively forceful, and ended without dribbling as soon as he ceased straining. He was found to have about an ounce of residual urine. He stated that he had no sensation of distension of the bladder, except abdominal discomfort when his bladder was full. He was conscious of the presence of flatus in the bowel and could succeed in passing it, or a motion, by straining. Experiment January 8, 1933.

Case 2.—Complete bilateral lesion of fifth lumbar and all sacral roots of the cauda equina, partial lesion of first four lumbar roots.

F. B., aged 22, admitted to the National Hospital on October 6, 1932, under the care of Dr. James Collier.

History.—Six months before admission crushed in a colliery accident with immediate complete paralysis of lower limbs, loss of sensation below the groins, retention of urine, and loss of control of bowels. After catheterization for six weeks involuntary micturition commenced. Some return of sensation over the front of the thighs commenced three weeks after the accident, and five weeks later some recovery of extension of both knees. He had regained no control over evacuation of the bowels.

Clinical state.—Weakness of lower abdominal musculature on both sides. All voluntary movements at the hip-joints weak except adduction. Flexion of both knees weak, extension powerful. No voluntary movement at ankles except faint dorsiflexion of the left ankle and inversion of the right ankle. The limbs lay extended with extreme wasting and flaccidity of all muscles, except the adductors of the thighs and extensors of the knees. The abdominal reflexes were present, the right knee-jerk absent, the left sluggish. Both ankle-jerks were absent and there was no response to plantar stimulation. The anal sphincter was patulous. There was diminution of all forms of sensation over the skin corresponding to the 2nd, 3rd and 4th and left 5th lumbar segments. Over the 5th lumbar on the right side and all sacral segmental areas on both sides there was complete loss of all forms of sensation (fig. 23). X-ray of spine shows fracture dislocation of 1st lumbar vertebra.

Micturition.—Preceded by the sudden onset of an unpleasant "desire to pass water," accompanied by an intermittent ill-defined sensation in the left groin, which lasted for several seconds and recurred about once a minute, until relieved by micturition. At first evacuation occurred inevitably immediately following the onset of this sensation, but by the time of the first experiment this sensation preceded micturition for three to five minutes, and by the time

of the second and third experiments for ten to fifteen minutes, being then accompanied by a sensation of swelling in the lower abdomen. He attempted to assist the passage of urine by straining and the stream started immediately. He was unable to terminate voluntarily the powerful stream which resulted. Such expulsion of urine occurred about once an hour; there was no dribbling. He had no knowledge of ability to pass urine without the presence of the sensation referred to the groin, and there was no sensation of passage of urine apart from relief from the sensation referred to above. He could pass a little

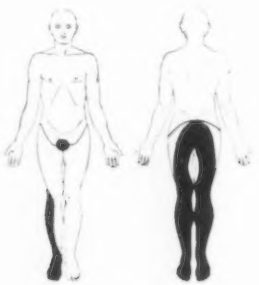

FIG. 23.

urine by straining without previous sensation. At the time of the third experiment he stated he had some slight sensation of the passage of urine (relief from previous sensation) and of the passage of the catheter through the meatus, although no recovery of sensation in the cutaneous areas of fifth lumbar and sacral segments had occurred. Experiments: October 15, November 13 and 27, 1932.

Case 3.—*Complete bilateral lesion of the third, fourth and fifth sacral roots, partial lesion of second sacral roots.*

G. G., aged 17, admitted under the care of Dr. Gordon Holmes on July 24, 1933.

History.—Having previously been in good health, towards the end of May he commenced to suffer from an ache over the sacrum, most intense in the mornings. Two weeks before admission he awakened with a numbness of the buttocks and perineum, he could not pass urine, and was catheterized at regular intervals from that time onwards. The numbness persisted. After forty-eight hours he commenced to suffer from bouts of burning pain in the backs of the thighs which occurred two or three times a day from that time onwards for two weeks. Three days after the onset of the numbness he first noticed weakness of the lower limbs which was slight and did not interfere with walking. At the time of his admission to hospital eight weeks after the commencement of his illness the cranial nerves, upper limbs and trunk showed no abnormality. There was no defect of motor power of the lower limbs with the

exception of some doubtful weakness of plantar flexion, no wasting and no fibrillation. The perineum bulged with respiratory and other abdominal movements. The tendon-jerks were all present and equal in the upper limbs, the abdominal reflexes were present and equal, the knee-jerks were both brisk and equal, the right ankle-jerk was present, the left absent, the plantar responses were flexor. No form of sensation was appreciated over the distribution of the 3rd, 4th and 5th sacral segments (fig. 24), and there was some impairment of all forms of sensation over the area corresponding to the 2nd sacral segment on both sides. Complete inability to pass urine. No sensation from the bladder except severe lower abdominal pain when distension became extreme. No sensation from catheterization. He had no control over the movements of the bowels. His urine was found to be grossly infected and the bladder was from that time washed out regularly. On July 31 examination of the cerebrospinal fluid showed an initial pressure of 60 mm. Jugular compression caused a slow rise and a slow fall. The fluid was clear and colourless and contained one cell per c.mm., total protein 0·2 per cent., globulin strongly positive. Wassermann reaction negative.

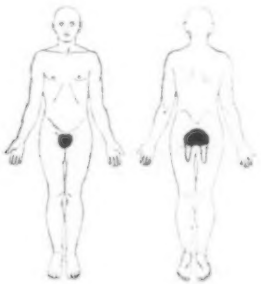

Fig. 24.

Three weeks before the experiment he found that after prolonged straining he could pass some urine. In the next two weeks he found that he could pass urine with a little less straining. He still had no sensation of moderate distension and no sensation of passage of urine, and during this two weeks the only indication of sufficient distension to allow passage with straining was the occurrence of involuntary dribbling which he was unable to prevent by voluntary effort. This dribbling would occur a number of times a day. In the week before the experiment voluntary evacuation of urine occurred much more easily than before, although he still had to bear down to initiate passage. At the same time the amount of involuntary dribbling became much less, though still occurring at intervals during each day. With such dribbling he had an unpleasant feeling of desire to micturate, which also was first felt one week before the time of the experiment.

Diagnosis.—Sacral neuritis.

Clinical state at time of experiment.—Careful examination could demonstrate no weakness of movement in either lower limb. A remarkable feature was the laxity of the perineum. A slight cough when the patient was in the prone position caused pronounced bulging of the perineum (S. 3, 4). He was unable to withdraw the perineum voluntarily. The glutei were of good bulk and contracted firmly on movement. The left ankle-jerk was still absent. Loss of sensation was still complete over the third, fourth and fifth sacral segments and partially over an area corresponding to second sacral segment. Experiment April 27, 1933.

Case 4.—Complete transverse lesion of the spinal cord at the level of the eleventh and twelfth dorsal segments with impairment of the tenth dorsal segment.

C. T., aged 35. Admitted to the National Hospital January 17, 1933, under the care of Dr. Adie.

History.—Accident September 3, 1931, with immediate loss of power of movement of lower limbs, of sensation below the level of the umbilicus and retention of urine. Commencement of involuntary flexion movements of left knee eight months after the accident and of right knee three to four months later. The upper level of the sensory defect had receded to the groins about eight months after the accident, and from that time there was no further recovery. There was no return of motor function. He had an indwelling catheter, through which his bladder was washed out daily for ten months. With removal of the catheter it was found that the passage of urine occurred spontaneously about once an hour. This occurrence was preceded for a very brief interval by the appearance of a palpable swelling in the mid-hypogastrium. Massage of the lower abdomen could at times cause the appearance of this swelling (contracting bladder) and bring about the occurrence of micturition which it invariably preceded. Spontaneous penile erection occurred frequently and was abolished by micturition. He had no voluntary control over defæcation, but had found that massage of the abdomen in the left iliac region occasionally induced it

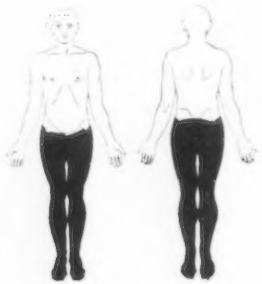

FIG. 25.

Clinical state.—Some weakness of muscles of lower abdominal wall. There was no voluntary power in the lower limbs, which lay extended with some increase in tone in extensors of both knees and plantar flexors of the ankles. There were occasional brief momentary spasms of flexion in both lower limbs. Arthritic changes in both knee-joints and both ankle-joints limited movement. Upper abdominal reflexes present, lower absent. Knee and ankle jerks brisk and ankle clonus present on both sides. Extensor plantar response on right side. Flexion of limb but no toe movement on stimulation of the sole of the left foot. There was complete loss of all forms of sensation below the tenth dorsal dermatome on the right side and eleventh on the left (fig. 25). Above this level there was some slight loss of sensation corresponding to the tenth dorsal segment (not shown in fig. 25). A scratch of the skin in any part of the lower limbs, from the first lumbar skin segment downwards, elicited reflex flexion of the limb stimulated. X-ray of spine revealed fracture dislocation of body of the tenth dorsal vertebra. There was a chronic infection of the urine. Micturition was periodic, forceful, abrupt in onset and cessation, and usually secured complete evacuation. It could be interrupted, often for long intervals, by reflex flexion. Experiment February 18, 1933.

Case 5.—Transverse lesion of the spinal cord, causing total destruction of second, third, fourth and fifth lumbar segments and partial affection of eleventh and twelfth dorsal and first lumbar segments.

D. McK., aged 28. Admitted April 20, 1933, under the care of Dr. Carmichael.

History.—Fourteen months before admission fell 30 ft. at sea with immediate complete loss of movement of lower limbs. According to the patient's statement he was not aware of any loss of sensation. He was unable to receive medical attention for three days. He stated that he had been incontinent of urine from within the first few days after his accident onwards. There was no sensation of distension, nor any control over urination or defæcation. He developed a sacral bed-sore. After some weeks the level of loss of sensation receded. Five months before admission small involuntary movements of the right lower limb commenced to occur, and within a short time involved the left lower limb as well.

Clinical state.—Weakness of the abdominal muscles below the umbilicus on both sides. There was no power of voluntary movement in the lower limbs, which lay extended with reduced tone in all muscle groups. The muscles of both lower limbs were wasted. There was a faint upper abdominal reflex on both sides, the middle and lower were absent. Neither knee-jerk could be elicited. Both ankle-jerks were present. There was no ankle-clonus. No reflex flexion or dorsiflexion of the great toes or of knee- or hip-joints could be obtained from any part of the limbs. A brisk anal reflex could be evoked from both sides, accompanied by some external rotation of the thighs and slight plantar flexion of the great toes. This reflex could be obtained from the segmental areas of the sacral segments, and is discussed in the text. There

was loss of all sensation below a level corresponding to the lower limit of the tenth dorsal segment on the left side and of the first lumbar segment on the right side (fig. 26). X-ray revealed fracture and partial collapse of the body of

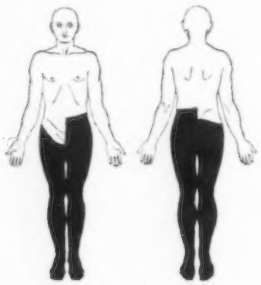

FIG. 26.

the eleventh thoracic vertebra. Lumbar puncture gave evidence of complete spinal block. Wassermann reaction of fluid was positive, but no evidence of inflammatory change.

Micturition.—No sensation of distension of bladder. Spontaneous abrupt evacuation at varying intervals up to two hours unaccompanied by sensation. Stream forceful without dribbling. He could commence micturition by straining down for about a minute, and if there had been an interval since the last evacuation almost any abdominal movement would be followed by the occurrence of micturition. Often evacuation was complete, but it was interrupted by stimulation of the sole of the foot and then seldom recurred within many minutes. Experiments May 27, August 27, September 2 and 10, 1933.

Case 6.—*Complete transverse lesion of the third dorsal segment of the spinal cord.*

H. S., aged 20. Admitted September 25, 1933, under the care of Dr. Gordon Holmes.

History.—On June 20, 1933, the patient's arms were drawn between heavy rollers, the forcible extension of his neck eventually stopping the machine. He sustained multiple fractures of his upper limbs, and on recovering consciousness thirty-six hours after the accident, he retained no sensation and no voluntary movement of the trunk or lower limbs. He was unable to pass urine, and until the date of admission to the National Hospital urine was passed through an indwelling catheter. He was incontinent of fæces and no recovery of motor or sensory functions occurred.

On admission he was extremely emaciated, the left pupil was smaller than the right and there was ptosis of the left upper eyelid. There was general wasting of the muscles of the arms, most marked in the intrinsic muscles of the left hand, but no complete loss of power. All muscles except the diaphragm

below the second intercostal muscles were completely paralysed. Both lower limbs lay extended, and spasms of involuntary flexion occurred from time to time, more often in the right leg than in the left.

The deep arm reflexes were all present, but more brisk on the right side. Transient, easily fatigued localized abdominal reflexes could be obtained. The knee and ankle jerks were brisk on the right, less active on the left. The hamstring jerks were very active. No ankle-clonus could be elicited. Plantar stimulation produced a brisk dorsiflexion of the great toe on the right side, a less brisk dorsiflexion on the left, as well as brisk flexion at knee and hip. Loss of sensation complete below D1 (fig. 27).

Stimulation of any part of either lower limb evoked reflex flexion at the hip, knee and ankle joints, brisker on the right side than on the left, occasionally with some flexion of the opposite limb. There was no obvious abdominal or perineal movement. The reflex could be obtained from the lower abdominal wall on both sides and from the glans penis: it required stronger stimulation

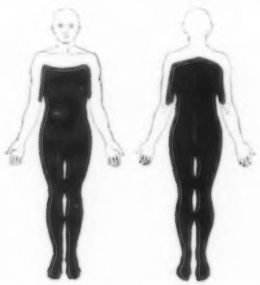

FIG. 27.

over the glans penis than elsewhere and over the left side than over the right. The perineum appeared indurated, probably as the result of the indwelling catheter, and no local response to scratching of the perineal skin was observed.

The musculature of the lower limbs was loose and atonic, apart from some heightened resistance of the flexors which persisted for a short interval after involuntary or induced reflex flexion.

The urine was grossly infected and was discharged in small dribbling quantities at irregular intervals. He was catheterized twice daily for purposes of vesical lavage and the vesical contents were found to vary from 84 to 280 c.c. Fluid run into the bladder was returned with moderate force when a volume of 280 c.c. was reached. Spontaneous defæcation occurred at intervals. He had no sensation of vesical distension, micturition or defæcation. There was no spontaneous sweating below the level of the lesion, but if covered by too many blankets profuse sweating occurred over the upper limbs, neck and head, and especially over the left side of the face.

On admission he was suffering from a profound general toxæmia with a

large sacral bedsore and from his condition he died on October 13, 1933. At autopsy the spinal cord was found to be completely softened in the region of the third dorsal segment. The spine of the second cervical vertebra was unduly prominent but no fracture was detected.

Experiment September 30, 1933.

We wish to express our indebtedness to Dr. Gordon Holmes for his constant interest and encouragement, and to the various members of the honorary staff of the National Hospital who have so kindly allowed us to investigate their patients.

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PERCEPTION OF FLICKER IN LESIONS OF THE VISUAL PATHWAYS.

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THE perception of flicker has received considerable attention in physiological laboratories, but hitherto has not been applied to the study of disease with the exception that Braunstein [1], in 1903, using an alternately black and white sectored disc, investigated flicker perception in cases of optic atrophy and optic neuritis (causes not stated), amblyopia, glaucoma, chorio-retinitis and hemeralopia. With central fixation he observed a decrease of flicker perception in many of these cases. The peripheral retina was not investigated, and localizing defects of flicker perception were not sought for. The present work is a preliminary study of the perception of flicker in cases of intracranial tumour.

The ability of patients to appreciate flicker has been estimated by the rate of light interruption at which a flickering light loses its flickering character and appears to the subject as a steady illumination. This rate of light interruption is critical and is known as the fusion frequency. It is profoundly influenced by the intensity of the light and the size of the area in which flicker appears [2]. It is also modified by the brightness of the background, by variation in the light or dark adaptation of the subject's eye, by the length of time the light is observed before a judgment is given as to whether it is flickering or not, and by the region of the retina on which the light is projected. It serves no useful purpose to the present problem to consider the quantitative aspects of these factors which influence the fusion frequency, since, with one exception, they have all been kept constant. The only variable has been the area of flicker. As this area increases the fusion frequency rises, the rise being greater, within limits, as the light is projected further into the retinal periphery.

It is now generally believed that this effect of increasing area is due to spatial summation in the retina [3]. Granit and Harper [4] have shown that central and peripheral retinal areas exhibit only quantitative

differences in summative effects. They have pointed out that these differences are supported by histological evidence. Opportunity exists for summation in the human retina between bipolar, horizontal and amacrine cells, and the quantitative differences between central and peripheral summation are no doubt due to their mutual relations and to the convergence of receptors through them on to the final common pathways constituted by the axones of the retinal ganglion cells.

Fusion frequencies of flicker, both in large and small areas, at selected points in the four retinal quadrants, have been examined in this work.

Apparatus.

Determinations of fusion frequency have been carried out in a room from which it was possible to exclude all sources of light except that from two 60 watt lamps placed 3 ft. apart and at equal distances on either side of a point 4 feet perpendicularly above the subject's head. The background consisted of a piece of blackened linoleum, 10 ft. by 12 ft., set in a frame and attached to the wall behind the flicker apparatus. The flicker apparatus (fig. 1) comprised

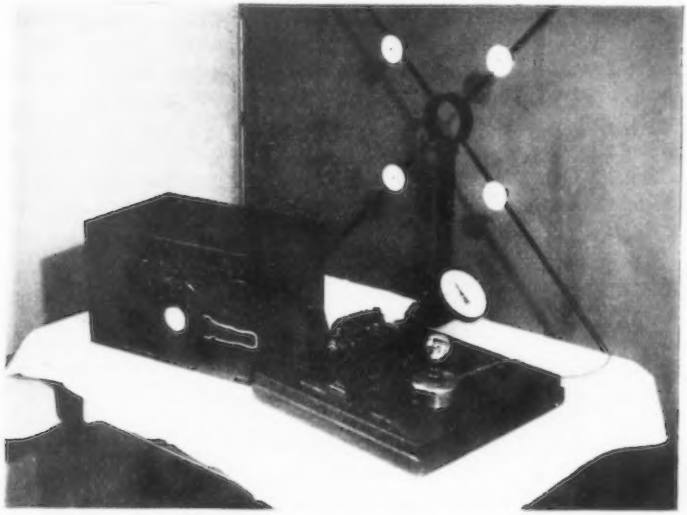

Fig. 1.—The apparatus used for determining fusion frequencies of flicker. The metal cover has been removed from the hardwood base to show the motor, the fan and the tachometer. In the background is the upright stand carrying four fixation discs.

a small electric motor connected by a belt to a fan attached to one end of a shaft mounted on two ball bearings. The fan had two 90-degree opposed vanes to give equal phases of light and darkness. Attached to the other end of the

shaft by a small spring coupling was an eddy current tachometer capable of recording on an illuminated dial the speed of the shaft from 5 to 30 revolutions per second. Immediately behind the fan was placed a 12-volt concentrated filament lamp mounted on a heavy lead base. This lamp was illuminated by a large capacity accumulator, the voltage from which was recorded by a Ferranti voltmeter and maintained constant by a small variable resistance. In front of the fan was mounted a Luc shutter to permit exposure of the light for any desired period. The whole apparatus was enclosed in a black-japanned metal cover. On the front of the cover and coinciding with the shutter aperture was an iris diaphragm and a milk glass screen. The diaphragm aperture could be varied to subtend visual angles of from one to four degrees at the subject's retina one metre away. The glass screen ensured by diffusion of light an equal light intensity over the whole area of the aperture.

Immediately in front of the diaphragm was a metal ring, 3½ in. in diameter, supported on a heavy stand resting on the floor. Through this ring the light beam passed to the subject's eye. Mounted on the ring at 90 degrees to each other and at 45 degrees to the horizontal were four rods carrying sliding pieces to which were attached white cardboard fixation discs. The sliding pieces could be moved along the rods to form angles of from 5 to 45 degrees with the light beam at the subject's eye.

The subject was seated at a table facing the apparatus, the chin resting on a metal support and the eyes one metre from the diaphragm aperture. With monocular fixation along the four rods the light beam could be projected to any desired point along the 45 degrees meridian of any of the four retinal quadrants. On a control table, out of the subject's field of vision, were centralized the light and power switches, the resistances for varying the motor speed, the shutter control and the voltmeters, and resistances for recording and controlling the background brightness and the intensity of the flicker beam.

Conditions of Experiment.

Selection of areas of light beam.—If the observed area of the light beam is too large the fusion point becomes less critical. As the fusion point is approached, using apertures of 4 degrees or over, the central area of the light may fuse early while the periphery continues to exhibit flicker. This effect is more marked for peripheral than for central perception of the light, and owing to spatial summation in adjacent retinal neurones this circumferential flicker may even be seen to extend beyond the edges of the light aperture. It was desirable therefore to use a small aperture in order to make a critical judgment of the speed at which flicker disappears from the area as a whole. On the other hand sufficiently large visual angles were necessary to be seen by patients who had field defects for small test objects. With small areas too the rise in fusion frequency with increase in area becomes considerably less, and it is obviously an advantage in detecting any defect of retinal summation that this rise should be as great as possible.

It has been found that the optimum range to satisfy these conditions lies between 1·5 and 2·5 degrees of visual angle. 1·5 degrees is greater than the largest test object used on the campimeter in this Unit, namely 50/2000 or 1·43 degrees, and can be seen 30 or 40 degrees in the periphery by patients with marked defects in the visual field contours for 10/2000 or smaller test objects. With the 2·5 degree aperture inexperienced subjects have little difficulty in making a critical judgment of the fusion point even when the light is projected far into the periphery. In any one subject repeated estimations of fusion frequencies of constant apertures have not varied from the mean result by more than one light flash per second. Under the conditions described here an increase of aperture from 1·5 to 2·5 degrees has, in normal subjects, increased the fusion frequency from between 8 to 12 light flashes per second, depending mainly on the region of retina illuminated.

Light adaptation.—The absolute value of the fusion frequency for any light of constant area and intensity varies considerably with the condition of light or dark adaptation of the retina. With central fixation and a dark adapted retina the fusion frequency may be 8 flashes per second slower than with the retina adapted to the standard background brightness described above. With 30 degrees paracentral projection of the light this difference may be as great as 12 flashes per second. In this work, as a preliminary to making estimations of fusion frequencies, each subject has been permitted 5 minutes adaptation to background brightness. This time has been occupied in demonstrating coarse and fine flicker and fusion for both 1·5 and 2·5 degree apertures.

Adaptation to flicker.—The retina quickly adapts to flicker, the rate of adaptation being more rapid in the periphery. This quality necessitates equal time exposures of the flicker beam in estimating its fusion frequency. Constant time exposures avoid apparently lower readings in the periphery. For example, a light of 1·5 degree aperture exhibiting coarse flicker became fused after 3 seconds constant fixation at 30 degrees in the periphery. With 10-degree peripheral projection of the light, adaptation is slower (7 to 10 seconds), and the flicker appears finer and finer during this adaptation period. It finally disappears, but an accurate judgment of the point at which it does so is difficult. Comparable results, therefore, demand constant periods of light exposure of less than 2 seconds. During this exposure the rate of light interruption must also be constant. Short periods of light exposure are of advantage since absolutely steady fixation is only required for a correspondingly short time. If fixation is not steady a light which is just fused may exhibit flicker at its margin and thus produce an apparently higher fusion frequency.

It is important that the period of light exposure should not be shorter than one second. Granit and Hammond [5], working with 1 and 3-degree apertures and a central and peripheral fixation, found that the fusion frequency rose from the onset of exposure, at first rapidly and then more slowly, finally reaching a maximum in rather less than a second. In the work described here equal exposures of one second duration were used and the subject was required to judge whether flicker occurred at any period of the exposure.

A definite judgment was usually given as to the presence or absence of flicker on a single exposure, and it was only rarely when the light was being projected well out in the periphery that a second exposure was requested or an indecisive reply elicited.

Fixation.—Before beginning estimations the blind spots were mapped out in order to demonstrate steady fixation and guard against pseudofoveæ. No cases in which central vision was interfered with have been included.

Results.

Normals.—Creed and Ruch state in a recent article [6]: "From the somewhat confusing literature we are probably justified in concluding that flicker is more marked in the periphery than in the centre of the field of vision with moderate intensities of illumination and objects of moderate size, but that the contrary may often be found with small objects (subtending less than 1 degree or 2 degrees) and with intense

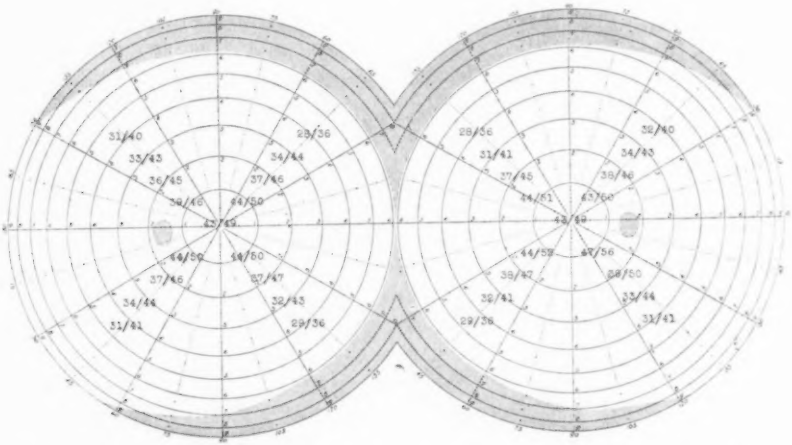

Fig. 2.—Fusion frequencies of flicker in a normal subject. Each pair of numbers represents the fusion frequencies of 1·5 and 2·5-degree light apertures respectively.

stimuli." This statement shows the necessity for controls in the interpretation of results, and in obtaining controls the experimental conditions modifying flicker must be constant throughout. A sufficiently extensive survey of the normal retina should be made to include possible regional variations in flicker not only from centre to periphery, but from quadrant to quadrant. This has been done by examining in some detail the perception of flicker in three skilled observers and in the

normal quadrants of patients with visual field defects. All factors modifying flicker were constant with the exception of the light aperture, which subtended an angle of either 1·5°, or 2·5° at the subject's retina. All four quadrants of each visual field were examined as far as 40° into the periphery. Seventeen points, 10° apart, were selected in the visual field of each eye, the fusion frequency for 1·5° and 2·5° apertures determined at each point and the results plotted on charts (fig. 2).

The results corresponded closely and confirmed several previous observations on flicker. There was always an increase in fusion frequency corresponding to an increase in area and this increase was, within limits, greater in the periphery. With the areas and light intensity used the fusion frequency for a constant aperture fell as the light was moved from 10° outward into the periphery, and also fell slightly as it was moved from 10° towards the fovea (fig. 3). This

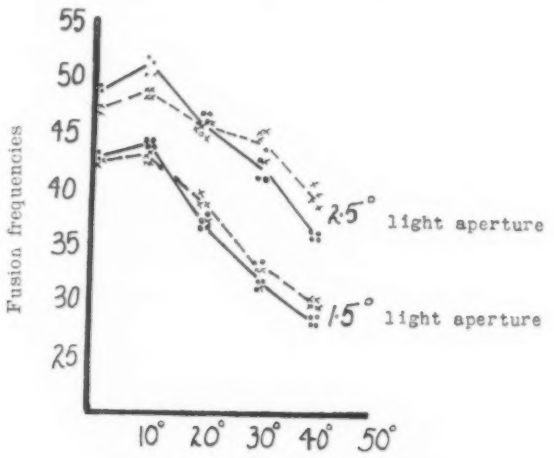

FIG. 3.—Fusion frequencies of flicker in the retinæ of two normal subjects.

Subject P.A.L.: + - - - - + - - - - + - - - - + Subject G.E.P.: ——·——·——·

observation has been made under different conditions by Granit and Harper [4], Creed and Ruch [6], and Lythgoe and Tansley [7]. It is due most probably to antagonism between receptor sensitivity and spatial summation. Summation is at a minimum at the fovea and increases with increasing convergence in the periphery. Receptor sensitivity is at a maximum at the fovea and appears to diminish pro-

gressively in the periphery. Summation increases the fusion frequency, while low sensitivity decreases it, and the point of minimum antagonism for a constant area and intensity appears to lie between the fovea and the 10° isopter. This point was not determined accurately since the points examined were 10° apart. It appears from fig. 3 that the highest absolute value of fusion frequency is at 10° from the fovea, but the value may rise higher somewhere between the fovea and 10° [7]. Between 10° and 30° spatial summation with increase in area becomes greater, or in other words the slope of the 1·5° aperture curve is steeper than that for 2·5°. With both apertures the fall in receptor sensitivity proceeds *pari passu*, while summation is facilitated by the larger area and thus the curves diverge. Beyond 30° the curves converge, probably due to the continued fall of receptor sensitivity after the maximum development of summation. In different individuals the absolute values of these curves may be slightly higher or lower but their mutual behaviour tends to be constant. The fall in the absolute value of fusion frequency beyond 30° was generally greater in the nasal fields (receptors innervated by the ipsilateral cortex) (fig. 2).

In the temporal fields there is a higher fusion frequency in the lower quadrants than in the upper. This observation is parallel with that made by Weymouth and others [8] who found that light perception was higher on the temporal and inferior meridians, and lower on the nasal and superior.

In determining the changes in flicker perception occurring in disease, the results shown in fig. 2 may be taken as a typical normal series. The maximum variation between any fusion frequency of this series and any other corresponding normal frequency determined under the same conditions is of the order of two or three light flashes per second. In disease the fusion frequency may be reduced by more than 50 per cent.

Chiasmal Group.

Case 1. *Large intrasellar Rathke pouch cyst.*—Th. D., male, aged 39. There had been progressive failure of vision in the left eye for two years, but no subjective disturbance of vision in the right eye. At operation on July 21, 1932, the tumour was removed completely, a procedure made possible by section of the left optic nerve.

Before operation there was no perception of light in the left eye, while in the right eye the visual acuity was $\frac{6}{9}$. The field of the right eye before operation is shown in fig. 4 and displays a full field for the 1·73 degrees test object and a temporal defect, more marked in the upper quadrant, for the 8·6 minute test object. There was marked primary optic atrophy in the left eye

with a deep cup and a well-defined lamina cribrosa. The right disc exhibited only very slight pallor.

On March 17, 1933, visual acuity was the same as before operation, but

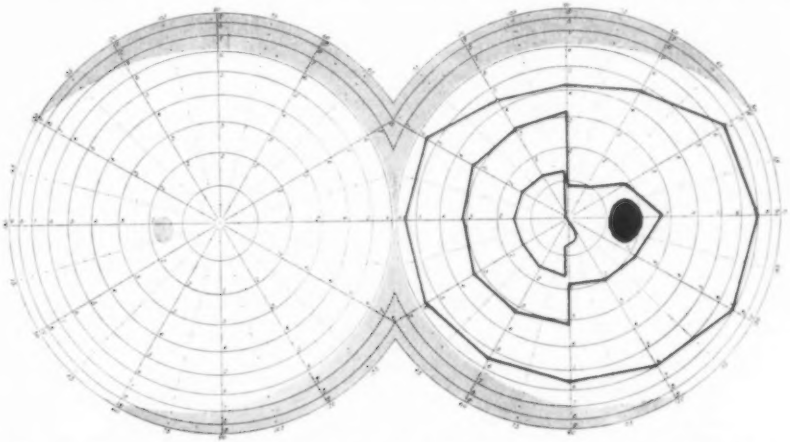

FIG. 4.—Visual fields of Case 1 one day before operation. Visual acuity of right eye $\frac{6}{9}$. Test objects: 1·73 degrees and 8·6 minutes, and 17·2 minutes (red).

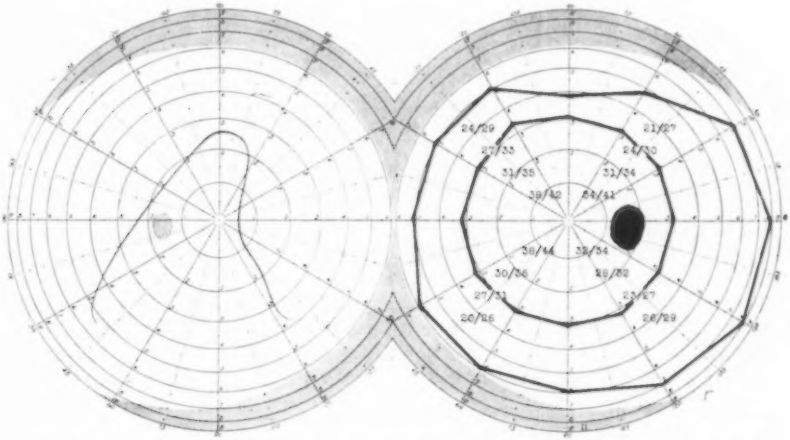

FIG. 5.—Visual fields and fusion frequencies of flicker in Case 1 eight months after operation. Central vision of right eye $\frac{6}{9}$. The fields are charted for 1·73 degrees and 8·6 minutes test objects.

there had been a recovery of the contours of the field for the 8·6-minute test object (fig. 5). Except for a slight fall of visual acuity and a slight pallor of the disc this eye might be recorded as normal. Even with a 1·7-minute test

object there was no field defect. In spite of this there was a fall in the fusion frequency of flicker in all four quadrants. Both 1·5-degree and 2·5-degree apertures were affected proportionally. As this benign lesion had been completely removed eight months previously the changes in flicker perception were evidently due to destruction of axones. This is in accord with the fact that, to judge from the endocrine disturbances, the lesion had been present for many years.

Another significant observation here and in other cases where there was chiasmal compression and evidence of optic atrophy was a local fall in fusion frequency between regions of higher frequency. In fig. 6 this local fall can

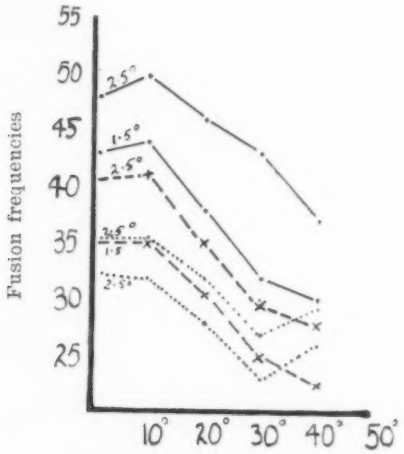

FIG. 6.—Fusion frequencies of flicker in the right eye of Case 1.
(Average curves of all four quadrants): + - - - - + - - - - + - - - - +
(Right lower temporal quadrant only): .....
Normal curves: ·——·——·——·

be seen at 30 degrees in the lower temporal quadrant where the fusion frequencies are lower than at 20 degrees or 40 degrees. This local fall is prone to occur in the quadrant or quadrants in which the general fall of fusion frequency is most marked, and is no doubt due to local axone destruction at the point of maximal pressure by the tumour.

Case 2. *Intrasellar cystic chromophobe adenoma of the pituitary gland.*—C. A., female, aged 55. There had been a history of visual disturbance for twenty years. She had had to wear glasses and the left eye was said not to be as good as the right. For eighteen months she had had difficulty in reading. At operation on December 20, 1932, the cyst containing 4 c.c. of fluid and its capsule were completely removed.

Before operation the fields and acuity were as in fig. 7, and there were signs of primary optic atrophy of both discs more marked in the left. The left eye was not examined for flicker because of the involvement of macular vision. In the right eye before operation flicker could not be perceived in the upper temporal quandrant, while there was a marked fall of fusion frequency for both apertures in the lower temporal quadrant, accompanied by a slight fall in the nasal quadrants (fig. 7.).

A fortnight after operation there was a marked improvement in the acuity and field of the right eye and flicker perception, though grossly impaired, had returned in the upper temporal quadrant. There was in addition a slight rise in the fusion frequency of both apertures in the lower temporal quadrant (fig. 8) and in the nasal field.

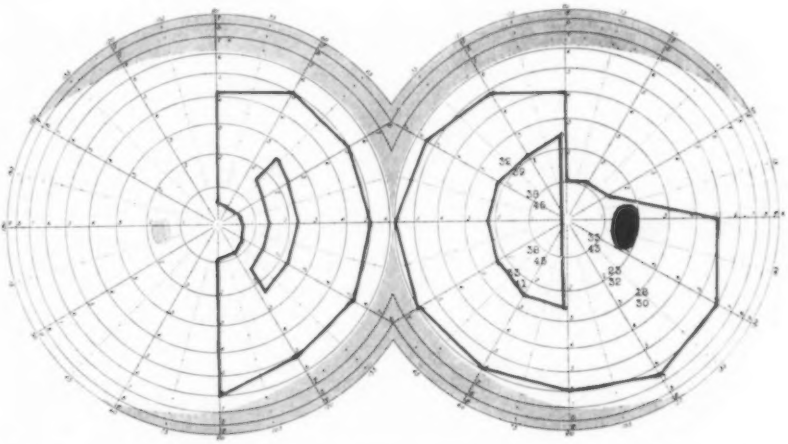

FIG. 7.—Visual fields of Case 2 one day before operation. Visual acuity of right eye $\frac{6}{36}$, of left eye $\frac{6}{18}$. Test objects: 1·73 degrees and 8·6 minutes.

The changes in fusion frequency observed in this case two weeks after operation are very closely allied to those observed in Case 1 eight months after operation, and in both cases, no doubt, there had been considerable axone destruction.

Case 3. *Chromophobe adenoma of the pituitary gland.*—P.M., male, aged 33. The tumour was removed subtotally on May 2, 1933. In this case there had been a complaint of failing vision in the left eye for twelve months. The patient had first noticed a "blankness" to the left of the left eye. He had had a "misty streak" in front of the right eye for four months before operation.

On examination there was severe primary optic atrophy on the left side with a well-defined lamina cribrosa. The right optic disc exhibited some pallor on the temporal side. The acuity was $\frac{6}{9}$ left and $\frac{6}{6}$ right, and the nature of the field defect four weeks before operation is seen in fig. 9. Fixation was unsteady

in the left eye. At this time flicker fusion frequencies in the right eye were diminished in the four quadrants, slightly in the nasal but more definitely in the temporal field. Both apertures were equally affected. There was a

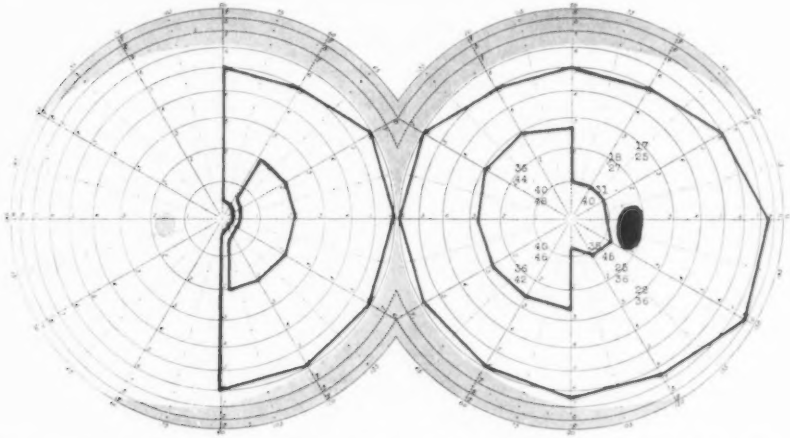

FIG. 8.—Visual fields and fusion frequencies of flicker of Case 2 fourteen days after operation. Visual acuity, right eye $\frac{6}{9}$, left eye $\frac{6}{6}$. Test objects: 1·73 degrees and 8·6 minutes.

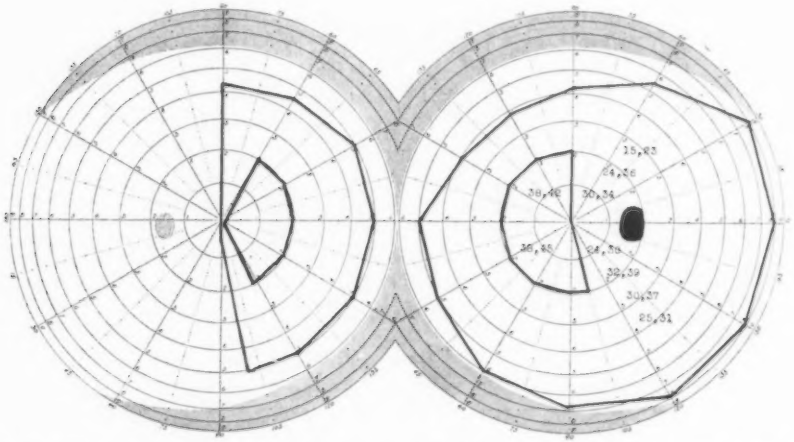

FIG. 9.—Visual fields and fusion frequencies of flicker in Case 3 four weeks before operation. Visual acuity of right eye $\frac{6}{9}$, of left $\frac{6}{6}$. Test objects: 1·73 degrees and 5·2 minutes.

marked local fall of fusion frequencies at 10 degrees in the lower temporal field. Two days before operation a central scotoma had developed in this area extending from the fixation point out to 10 degrees. Thirteen days after opera-

tion the visual acuity was $\frac{6}{9}$ in both eyes, and the visual fields had recovered considerably (fig. 10). Fixation was still unsteady in the left eye. In the right eye the fusion frequencies in the temporal field were much higher than before operation, and at 10 degrees in the lower temporal quadrant, where there had been the scotomatous defect suggesting a rapid advance in the lesion (9), the fusion frequencies were not very much below normal. This suggests that here the rapidly increasing pressure had impeded conduction without actually destroying the nerve-fibres. In the nasal field of the right eye there had not only been no improvement of flicker perception, but the fusion frequencies, especially for the larger aperture, had fallen slightly. The explanation here may have been that in some fibres which had been under pressure for a long

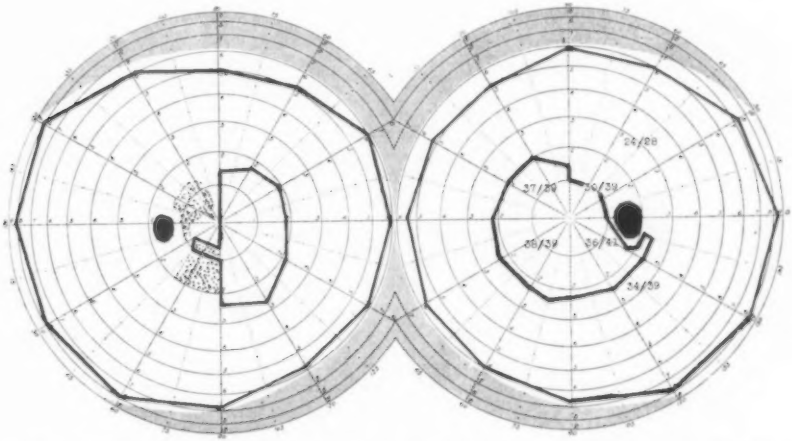

FIG. 10.—Visual fields and fusion frequencies of flicker in Case 3 thirteen days after operation. The fields are charted for 1·73 degrees and 5·2 minutes test objects. No trace of relative scotoma in right temporal field. Occasional scotoma in left temporal field near macula. Central vision $\frac{6}{9}$ in each eye.

time actual degeneration had finally taken place. Such degenerative changes would greatly diminish retinal summation, and thus the larger area would be more affected.

Case 4. *Chromophil adenoma of the pituitary gland.*—J. O. H., male, aged 29. The tumour was subtotally removed on April 11, 1933. The history and acromegalic appearance of this patient indicated that the tumour had been present for some years, and at examination two years before operation a slight upper bitemporal defect of the small isopters was observed. Subjective visual failure, however, only appeared five months before operation. On examination there was slight temporal pallor of both discs, rather more marked on the left side. Visual acuity was reduced to $\frac{6}{9}$ in the right eye and $\frac{1}{9}\frac{1}{5}$ in the left. There was a bitemporal defect, scotomatous in the left eye and peripheral and central

in the right (fig. 11). The examination of flicker perception was precluded by the impairment of macular vision in both eyes.

Fourteen days after operation there was a considerable recovery of the

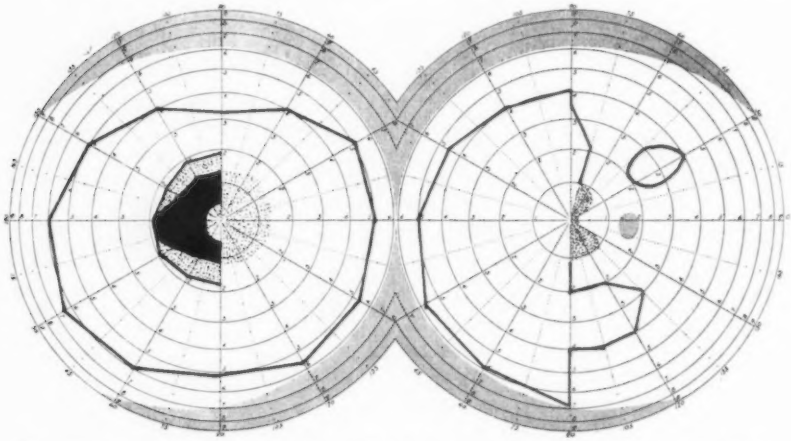

FIG. 11.—Visual fields of Case 4 immediately before operation. Visual acuity of right eye $\frac{6}{9}$, of left eye $\frac{1}{12}$. Test object: 1·73 degrees.

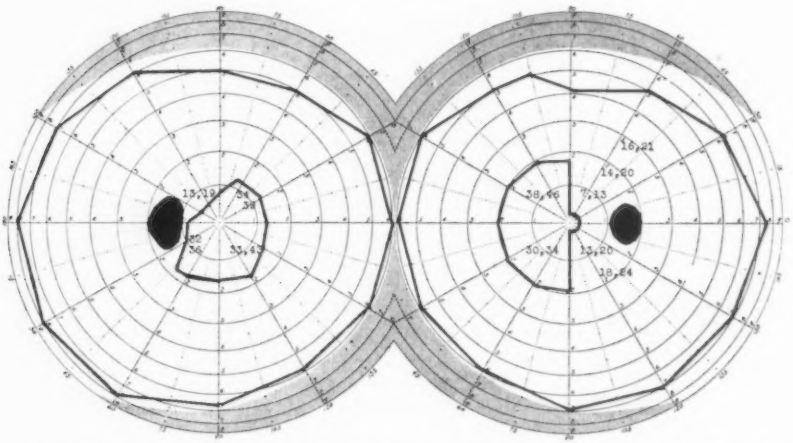

FIG. 12.—Visual fields of Case 4 showing fusion frequencies of flicker fourteen days after operation. Visual acuity of right eye $\frac{6}{9}$, of left eye $\frac{6}{9}$. Test objects: 1·73 degrees and 5·2 minutes.

visual fields, and the visual acuity was $\frac{6}{9}$ in each eye. The bitemporal defect could only be demonstrated by small test objects (fig. 12). Flicker perception was diminished in all four quadrants in both eyes. There were profound local

falls in fusion frequency close to the temporal side of each macula, except at 10 degrees on the left lower temporal quadrant, and there was a rise toward the normal in the region of the temporal island in the right eye. Both apertures were affected equally. Here again the scotomatous nature of the visual defect suggested rapidly advancing axone compression, and after the relief of pressure the most marked flicker defects persisted where axone destruction had been greatest. When a tumour has only been partially removed (Cases 3 and 4) the remainder of the tumour is still able to produce some tension which may result in "decremental conduction."

Four other cases of chiasmal compression have been examined for flicker defects and they all confirm the results described in this section.

From these observations the following conclusions may be drawn about the effect of chiasmal compression on flicker perception. (1) Flicker perception is diminished; (2) this diminution may occur in the absence of any defect in the visual field (Case 1); (3) large and small areas are approximately equally affected; (4) the flicker defect generally appears to some degree in all quadrants of the visual field; (5) there are usually marked local falls of fusion frequency of flicker in the quadrant or half field most profoundly affected.

Suprachiasmal Group.

Flicker perception was examined after operation in four cases of parietal tumour in which the visual fields and acuity were normal. In two cases, both of them calcified gliomas, flicker perception was normal. In another, an extensive left fronto-parietal cystic tumour, flicker perception was impaired in the right homonymous fields, but was normal elsewhere. In the fourth case, after removal of a huge right parietal meningioma, flicker perception was impaired throughout the left temporal field only, the left nasal and the right half fields showing no abnormality.

These observations are obviously too few to justify any conclusions being drawn, but they indicate that flicker perception may be diminished in suprachiasmal lesions and that this defect may occur in one or both of the contralateral half fields in the absence of any defect for form. The degree of dissociation may be so great that a light and its circular form may be appreciated in the periphery without any appreciation of flicker even at very slow rates of light interruption. The few observations so far made indicate that in suprachiasmal lesions, in contradistinction to the chiasmal group, flicker in small areas is more affected than flicker in large areas.

These observations suggest that there is a dissociation between flicker

perception and the form-movement perception of perimetry. No conclusions as to its cause are justified without further work.

These observations on flicker perception are preliminary to a more thorough investigation of the several problems which arise out of them. This field for research which has been revealed by the quantitative investigations of Ragnar Granit and his co-workers on flicker is extensive, and owing to the scarcity of suitable cases information that may prove valuable to the clinician can only follow an intensive survey of a larger series of cases. This introductory paper is submitted in the hope that such investigations will follow.

The author is deeply indebted to Mr. Hugh Cairns and Dr. Ragnar Granit for assistance.

The expenses of apparatus were defrayed by the Charles Bingham Bolton Fund for Neurology.

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LEIODYSTONIA, AN ENDOCRINE-AUTONOMIC NEUROSIS OF THE TROPICS.

BY P. M. VAN WULFFTEN PALTHE,

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LEIODYSTONIA is a malady which is characterized by a disturbance in the regulation of the vegetative functions, and especially by a lability in the tonus of the involuntary muscles. For clinical purposes the name leiodystonia[1] will serve as it summarizes the essential symptoms without prejudice to the still uncertain causes of the malady. French clinicians [1] have given the name "léiasthénie" to analogous conditions; they have also spoken of "*asthénie des muscles lissés.*" As leiodystonia is not identical with the *léiasthénie* of the French the latter name cannot be employed.

Its chief characteristic is a variability of the tonus of the involuntary muscles. It is true that this lability of tonus generally occurs on a low hypotonic level, but other symptoms are due to a spastic dystonia. For the same reason it is less desirable—as I myself did in a previous article [2]—to name the malady after one of its symptoms. In leiodystonia the blood-pressure is nearly always low, but it may be sometimes high; this is a feature of the disease.

Leiodystonia is not a continuous disease but rather a constitutional inferiority called into being, or at least accentuated, by a long residence of Europeans in low-lying tropical country. The symptoms appear and disappear according as unfavourable or favourable factors predominate. It has been possible to study it in a large number of patients during the last seven years.

SYMPTOMATOLOGY.

A prominent symptom is the low blood-pressure; the systolic pressure fluctuates around the 100 mm., the diastolic around the 50 mm., not only in youthful persons but also in patients between 40 and 50 years of age. The action of the heart is tumultuous. Sometimes there

[1] Leiomyodystonia would be more correct, but as by tonus, muscle tonus is generally understood, the omission of the adjunct "myo" is justified.

is a slight enlargement towards the right and an accentuated second pulmonary sound. Vascular murmurs can be frequently heard over the larger arteries.

The patients have often a peculiar facial expression owing to their dilated pupils and the whiteness of their skin. The cutaneous blood-vessels are very sensitive to mechanical and emotional influences, and flushings and red patches come and go, more especially on the neck. Frequently there is slight œdema, not of the subcutaneous tissue but of the superficial layers of the skin over the tibiæ. Visceroptosis is common and the stomach is frequently filled with air owing to aerophagy. Attacks of profuse perspiration without cause, and of watery diarrhœa without pain, alarm the patient, and uncontrollable fits of sneezing may keep him awake all night. Epileptiform convulsions, sometimes followed by transient hemiplegia, are not rare. Finally, most patients become sexually impotent.

The chief subjective symptoms are headaches, lassitude, giddiness and insomnia, or, on the contrary, excessive drowsiness. Pains, especially in the chest and over the heart or between the shoulder-blades, and, in the case of women in the lower abdomen, an empty weak feeling in the stomach accompanied by palpitation of the heart, attacks of terror, with sensations of sinking away, of dying or of becoming insane, are very common. Singing in the ears and cloudiness of vision add to the patient's misery, and as a result he loses his self-control, becomes irritable and has sometimes uncontrollable fits of weeping.

The history of a typical patient may give a better picture of the disease than such a dry summary of subjective and objective symptoms.

A man, aged 46, came to the Dutch East Indies in his 30th year. In Holland his health was always excellent, but after some years in the tropics he began to feel less well. His own opinion was that he has become "nervous." This opinion he based on the fact that his symptoms were variable, for sometimes he felt well and fit for anything, but at other times he was perfectly miserable. He had then a sensation of being strangled and his heart beat violently, or rather his whole body palpitated, not only his heart. He became giddy, had a feeling as if he were sinking away, a feeling which terrified him: "I feel as if I were dying." This type of attack alternated with periods of extreme lassitude, and if he did not fight against it he could do literally nothing, even to lift his arm demanded too great an effort. If he struggled against it the attack of lassitude quickly passed off. When subject to these attacks he slept abnormally long and soundly, not only during the night but also by day. Every now and then he had attacks of profuse perspiration. Another troublesome symptom was that at the most inconvenient moments, and without any

definite cause, his eyes filled with tears and he had uncontrollable fits of weeping. As he had also pains all over his body and especially a violent pressure in his head, it is not surprising that this man, who had hitherto always done his work well although he had lately had some difficulty in concentrating his thoughts, should finally become desperate and call in medical help. It was, however, his wife who insisted upon it, as the patient thought it unworthy of a man to go to a doctor with such vague nervous complaints.

On examination there was no evidence of serious organic disease. The patient was a well-built man; his heart, lungs and kidneys were normal. The tendon reflexes were brisk. The pupils, which were remarkably wide, reacted promptly but insufficiently to light or on convergence, and quickly dilated again though the stimulus persisted. The retinal arteries were dilated almost as wide as the veins, and the discs were somewhat rose-coloured. No other changes were visible in the fundi. The most pronounced changes were found in the peripheral circulation; red spots and flushes were everywhere visible, more especially where his clothes had pressed. If a hand was laid for a single moment on his back a clearly visible impression of it in white was seen. A light touch was sufficient to cause a contraction of the cutaneous capillaries, a contraction which quickly passed into relaxation, for after a few seconds the mark became red. This peculiar dermography was still more striking when the skin was stroked with the handle of the percussion-hammer: first a white line appeared which immediately became bright red and was bordered by white rims, each about twice as broad as the central red line. Irritation of the skin anywhere was followed by alternate cramp and paralysis of the cutaneous blood-vessels. Red spots also appeared spontaneously.

The blood-pressure of this patient, whose heart was perfectly normal, was remarkably low for a man of his age. When we first took it after having adjusted and increased quickly the pressure in the armlet, thus exercising a strong stimulus on the arterial wall, the maximal pressure was 115 mm. Hg, but later, by avoiding as much as possible stimulation of the arterial walls, the systolic pressure fluctuated between 95 and 105, and the diastolic between 55 and 60.

From this description it is obvious that each of the various complaints and objective symptoms had in itself little that was characteristic; looking at them separately one might conclude, and it has been done too frequently, that the patient was an ordinary neurasthenic. But this man did not show the usual neurasthenic attributes; he regarded his complaints calmly and objectively, they were not an integral part of his personality nor bound up with it, and they exercised no continuous influence on his thoughts and actions, in short, there was no neurasthenic "character." It was necessary to compel him to go to the doctor, and he came accompanied by his wife, who had to urge him to say what he felt, because he was really ashamed of his symptoms, which he regarded

as nervous. In short, he was the antithesis of the "man with the notebook" in which all complaints are precisely described in case the patient should happen to forget a single one. He did not pity himself, he felt it annoying to be ill, he accused neither persons nor circumstances, and did not ascribe his illness to "overwork." In short, he regarded his illness as something essentially strange, a temporary disorganization which he thought would disappear when he was in other circumstances. Something quite different, therefore, from the chronic neurasthenic, the "homme à petits papiers" who runs from one doctor to the other and cherishes his symptoms as valuable weapons in the struggle of existence; the terror of all neurologists even in the tropics.

Too much emphasis cannot be laid on the fact that one should never diagnose leiodystonia from any of the separate symptoms described above; not one of them, not even the low blood-pressure, is pathognomonic. It is true that the blood-pressure is always low, or it might be better to say that it fluctuates at a low level, but we must not see in every low blood-pressure a leiodystonic disturbance. In perfectly healthy persons a low blood-pressure may be sufficient for the circulatory requirements. In genuine leiodystonia, under favourable circumstances (for example, a sojourn in the mountains) all the symptoms may disappear, but the blood-pressure does not change.

It is not necessary in order to diagnose leiodystonia that all these complaints and symptoms should be present simultaneously and in equal intensity. This is rare, for generally one group of symptoms predominates and the others become apparent only after long observation and patient inquiring. These symptom-complexes, which are sometimes so dominant that they are described as special diseases, must now be dealt with in greater detail.

The feelings of terror.—This is described by the patient as a sensation of sinking away, of dying, as if life were flowing away; sometimes also as if his mind were going and he was becoming mad. There is a real terror of death and is felt as such by the patient. It occurs particularly when the patient is at rest, and not under the influence of psychic and physical stimuli. The attacks are preceded by a sensation of giddiness and of palpitation throughout the body. In this state the blood-pressure is extremely low and vascular murmurs are audible everywhere. Everything indicates that the circulation is insufficient owing to a leak in the peripheral arterial system and congestion of the veins. There may be real danger to life. Then comes the feeling of terror, which may perhaps be regarded as a useful biological

reaction, for as a result of it substances are secreted into the blood which increase the tonus of the vascular walls and thus raise the circulation to its old level. One thing is certain, that the feeling of terror arises when it is necessary and disappears when the danger is over. It lasts only a short time and afterwards the patient feels better than he did before. The circulation also improves. Between the attacks the patient has no fears; he suffers as little from an anxiety neurosis as he does from neurasthenia.

The ocular symptoms.—The widely dilated pupils give the patient a peculiar appearance. To a strong light and on convergence they contract quickly but only in a slight degree, and even if the stimulus is continued they dilate again immediately. Loeper and Bauman [1] regard this as a constant sign in their "leiasthénie." In my cases it was seldom absent.

Symptoms of asthenopia are common and the patients complain of the disagreeable effect of bright daylight. In a few cases the optic discs were pinkish and the arteries in them were dilated, but never to such a degree as to suggest a choked disc such as Flandin and Gallois [3] have described.

Gastro-intestinal symptoms.—The gastro-intestinal symptoms commonly associated with leiodystonia often have an organic character, and consequently the patients usually call in a general practitioner or visit an internist. It is certain, however, that in the early stages at least there is no organic lesion. No matter how closely the symptoms may resemble those of gastric or duodenal ulcer, colitis or sprue, closer inquiry shows that the special features of these diseases are absent. No trace of inflammation or other changes, as atrophy of the mucous membranes, can be found. The changeable nature of the symptoms and the sudden cure which frequently follows a change of climate, also indicate the functional character of these symptoms.

These symptoms can be attributed to a hypersensibility of the autonomous reflex system of the intestinal tract. Some have a spastic character suggesting colitis spastica, and others are due to lack of tone, as the enlarged dropped stomach. There are also anomalies in the movements and the secretions of the intestines; obstinate constipation alternates with watery diarrhœa, without tenesmus and without mucus or blood. This hyperexcitability is clearly demonstrated by the reactions of the patients to slight and harmless stimuli; the first whiff at a cigar makes him giddy and induces an inclination to vomit, and a mouthful of coffee makes him hasten to the water-closet.

The patients have a number of other complaints of a more subjective nature. A disagreeable feeling of looseness, emptiness and heaviness in the stomach torments him at the most inconvenient moments, a feeling as if he were hollow and hungry frequently follows a meal which he has thoroughly enjoyed. In such a condition the stomach is filled with air and there is a moderate meteorism. If they are observed unawares it may be seen that these patients frequently swallow air, an action of which they are not conscious and consequently deny. It seems that the stomach distended with air is more comfortable than the feeling of loose emptiness, although it produces all kinds of discomfort later on.

This intestinal syndrome is often associated with cardiac and vascular symptoms, which is by no means surprising in view of their common origin. Organic affections of the intestinal tract, as colitis or chronic appendicitis, may determine the appearance of leiodystonic symptoms in other systems.

Cardiac and vascular symptoms.—The vascular syndrome is the most characteristic feature of leiodystonia. The low level and the variability of the blood-pressure is the symptom which attracts most attention, as it is the one which can be determined most clearly and objectively. This low, fluctuating blood-pressure is never absent, but one must not be satisfied with taking the blood-pressure once, and no conclusion should be drawn from the first visit to the doctor, when the pressure readings are often 10 to 20 mm. above their real level.

The vascular syndrome in leiodystonia, however, does not consist in a low blood-pressure only. The heart beats tumultuously, as in beri-beri, although the impulse is diffuse. In a few cases there is a slight enlargement to the right and an accentuated second pulmonary sound. The pulse is generally rapid and forcible. Murmurs can be heard over the larger arteries, as the femoral. Complaints of palpitation, inability to breathe deeply, pains in the chest and in the region of the heart, are common. All these symptoms resemble the circulatory disturbances in beri-beri, as described by Wenckebach and Aalsmeer [4]. The resemblance becomes still more striking as in leiodystonia too the circulation is paradoxically influenced by adrenalin. After an injection of 1 or $\frac{1}{2}$ c.c. of a 1 : 1000 adrenalin solution, the heart begins to beat more tumultuously; the systolic blood-pressure remains the same or diminishes a little, but the diastolic falls until it can no longer be measured. The pulse is rapid and firm. Murmurs can be frequently heard over the smaller arteries, as the radial and dorsalis pedis, and over the larger

arteries, as the femoral, they become very loud and acquire the sharp character of a pistol-shot.

A European, aged 26, who had already been five years in the tropics, during the last year began to be troubled with giddiness and attacks of faintness. He also complained of singing in his ears and at times of dimness of vision. A sensation of sinking away preceded short periods of absolute unconsciousness. Extreme lassitude, unnatural drowsiness, vague pains in his head and occasional palpitations completed the picture. All these symptoms became much worse when he took no exercise.

The objective symptoms were dilated pupils, white-rimmed red dermography, rapid pulse, brisk reflexes and slight pretibial œdema. The heart was not enlarged and its sounds were normal. The systolic blood-pressure varied between 150 and 130; the diastolic remained at 75. Directly after an injection of $\frac{1}{2}$ c.c. of a 1 : 1,000 solution of adrenalin the blood-pressure was 145/90, after five minutes it was 145/75, after ten minutes 140/30, and after fifteen minutes systolic was 140, and diastolic could not be measured. Loud murmurs of pistol-shot character were audible over the brachial and crural arteries. The action of the heart was agitated, there were generalized palpitations and the visible veins were congested.

Latent leiodystonic disturbances may be revealed by enfeebling illnesses or intoxications. One cigar, even the first pull at a cigar, may produce giddiness and an inclination to vomit, cloud the consciousness and induce palpitations.

The question arises whether the similarity between the functional circulatory disturbances in leiodystonia and in beri-beri has a deeper significance; in other words whether they are both—though perhaps in a different degree—due to one and the same mechanism. Wenckebach [5] has suggested that the circulatory disturbances in beri-beri are due to two factors, viz., a dilatation of the smallest ramifications of the arterial system and consequently a flooding under high pressure of the veins and the right heart, and secondly a degeneration of the heart muscle.

Degeneration of the cardiac muscle does not occur in leiodystonia and therefore the circulatory disturbances associated with it have never serious consequences. The former factor, however, by which the scuppers of the arterial periphery are opened, is present in the case of leiodystonia; in this respect the circulatory disturbances in leiodystonia are identical with those of beri-beri.

The cerebral symptoms.—Cerebral symptoms appear in three forms: (1) As migraine; (2) as short periods of unconsciousness with or without convulsions; and (3) as loss of consciousness followed by a

transient hemiplegia. In earlier articles [6] I have shown that such an attack of hemiplegia in a young person, without organic disease of the heart, vessels or kidneys, with a low blood-pressure, in the absence of syphilis and with nothing to suggest a tumour, multiple sclerosis or encephalitis, must be due to functional circulatory disturbances in the brain. This temporary disturbance is due to the association of cerebral vascular spasm with a low blood-pressure. Descriptions of a few cases may make this clearer.

The first patient was a young man, aged 24, who came to the Dutch East Indies for the first time two years ago. According to information supplied by those who knew him, he had already had several fits of "unconsciousness" which lasted from one and a half to two hours, and which were not accompanied by convulsions or spasms. He could say little more about these attacks than that they began with a sensation of cold and giddiness. A doctor who was called in when he was seized with the last attack had him removed to the hospital.

On examination, he had a left-sided hemiparesis, including the lower muscles of the face. With his left arm he could perform a few awkward movements only. Deep sensibility and stereognosis were disturbed in the left hand, in which there were also violent spontaneous pains. The abdominal reflexes could not be elicited on the left side. The left leg was also paretic and its tendon reflexes were exaggerated with ankle clonus; the reflexes of Babinski and Rossolimo were positive. The patient was dysarthric and stuporose, and complained of headache.

This was a classical example of a hemiparesis, the result of a lesion in the region of the right internal capsule extending into the thalamus. Further examination revealed no organic disease; his heart and blood-vessels were normal, his blood-pressure was low and the functions of the kidneys were unaffected. There were no signs of increased intracranial pressure. His temperature was normal. The patient denied venereal infection, and the Wassermann reaction in the blood and in the cerebrospinal fluid was negative, as was also Nonne's reaction. There was no pleiocytosis.

Formerly he had never been really ill. He did not drink, but smoked excessively. His occupation necessitated a busy, hustling existence. The heat where he worked in Priok Harbour (Java) is unbearable, and he ascribed his attack to it. Within twenty-four hours all his symptoms had disappeared, and he had become quite clear mentally. The following day he was up and about, but was still ataxic in his left arm and complained of spontaneous pain in it. The pathological reflexes in the left leg had disappeared but his face was still asymmetrical.

Two months later, after working for a long time in the heat, he was proceeding homewards on his motor-bicycle when his right side became paralysed and he fell. This hemiparesis lasted about an hour and had disappeared when

we saw him. He was still a little drowsy and spoke with difficulty, but what immediately attracted attention was symmetrical snow-white discolouration of his legs to the middle of the calves. His feet and the lower part of his legs were cold and he complained of violent pain in them.

There was obviously a disturbance of circulation in the brain combined with vascular cramp in the legs. This vascular cramp recurred in the course of the following months when the patient was on his way to Holland and caused, when he was on board ship, gangrene of one of the toes. In Holland he gradually improved (according to the patient, this was due to his having stopped smoking) and he returned to the Dutch East Indies apparently cured. He lived now very quietly, had easier work, neither smoked nor drank, and everything went all right until he participated in a rather "wild" night. Emerging from a night club he collapsed, vomited and was unconscious for half an hour. When he recovered consciousness his right side was again paralysed and he was unable to speak. On this occasion also the hemiplegia disappeared in about twenty-four hours.

Another patient was a man, aged 38, who has been ten years in the tropics. He came under observation in 1927 owing to complaints of lassitude and impotency. There was no organic disease, but his blood-pressure was very low (about 100 mm. systolic). The vasomotor system was very labile: he complained of dead fingers when swimming, attacks of profuse perspiration and watery diarrhœa. In the beginning of 1932 he had his first stroke, which began with headache, giddiness, vomiting, walking like a drunken man and repeated attacks of unconsciousness which he spoke of as "falling asleep." The doctor then consulted found facial paralysis on the left side, dysarthria, increased reflexes and a hard pulse. As he did not know the previous history of the case and the blood-pressure was 200/140, he diagnosed an angiospastic lesion as a result of essential hypertension. Within a few days all the symptoms vanished and the blood-pressure was 100/30. Fourteen days after this attack I was able to examine the patient and found typical leiodystonic symptoms. The systolic blood-pressure was 96 and the diastolic 56. The reaction to adrenalin was slightly but unmistakably paradoxical.

This attack was followed four months later by a second, much slighter and of shorter duration.

This patient is interesting for two reasons; in the first place because he is a very moderate smoker, and secondly, because immediately after the first stroke his blood-pressure was for a short period greatly increased as compared to its usual low level. I believe that heavy smoking combined with a general lability of the autonomic nervous system is one of the factors that can bring about these transient attacks of hemiplegia, but Külbs [7] certainly goes too far when he sees in the abuse of nicotine the only cause.

A raised blood-pressure during and immediately after a stroke is

common in "ordinary" apoplexy and indicates the extraordinary reflex sensitiveness of the vascular walls. It has been suggested [8] that this is a reaction on the part of the body to maintain, by means of the increased pressure, the circulation through the contracted cerebral arteries.

I have seen at least ten leiodystonic patients with cerebral symptoms such as are described above. In some of these angiospastic conditions in certain parts of the body, as white discolouration of the legs and dead cold fingers, alternated with general vascular atony. The combination of the two factors—spasm of the cerebral arteries and low blood-pressure—must be held responsible for the cerebral lesions.

All the symptoms which have been described separately in the ocular, the intestinal, the circulatory and the cerebral syndromes, together with the mental and physical abnormalities revealed by examination, should be regarded as a whole; they characterize one disease, leiodystonia, which in intensity and frequency reaches its height in the tropics. No one group of symptoms can be regarded as distinct or described as a special disease, however strange it may seem to place diarrhœa and hemiplegia, wide pupils and headache, in the same pathological unit.

As already said, leiodystonia is a latent constitutional inferiority which becomes manifest under certain unfavourable circumstances, and which disappears totally or partly when the factors which determined its manifestations have ceased to exist. Many arguments might be advanced to show that long residence in a tropical lowland may cause certain changes in the vegetative functions, and in particular in those predisposed to the malady called leiodystonia. This predisposition may exist in Europe as anomalies of the vegetative system, and in the tropics persons so affected may quickly show signs of leiodystonia. Vulnerability to tropical influences may also be acquired, and may be caused not only by the heat but also by an unhygienic manner of living (little sleep, excess in alcohol and tobacco, and little physical exercise), or by exhausting illnesses.

Various investigations have been made in the disturbances of the vegetative functions of Europeans living in the tropics; Radsma [9] found that the daily fluctuations in the carbonic acid content of the alveolar air was much greater than in temperate zones. In the afternoon there is an increase between 4 and 5 o'clock, and in the morning generally a diminution. Also the range over which the CO_2 tension varies in each individual is also greater than in Europe.

Radsma [9] also found that the reaction of the morning urine, in the case of Europeans in the tropics, is much more alkaline than in Europe. This shifting reaction is totally absent with the native population.

Neuhausz in 1893 showed that the average body temperature in the tropics is higher than in temperate zones. Radsma, who examined the daily temperatures of seventeen young Europeans, was able to confirm this. He found that smoking a single cigar increased his own temperature a few tenths of a degree.

The basal metabolic rate in Europeans in the tropics is also lower than in temperate climates. Knipping [13] found an average of −6·5 per cent., Teding van Berkhout [12] of −5·4 per cent. Benedict and Williams of −3 per cent., as compared with the standard figures of Harris and Benedict. Radsma also found the rate on the average 6 per cent. lower. This lowering of the basal metabolism cannot be ascribed to reduced albuminous nutriment. All indications go to show that it is brought about, directly or indirectly, by climatic factors.

Very little is known of the influence of the tropics on the blood-pressure of Europeans. Kiewiet de Jonge [10] found it was lower on the whole, but he was careful in coming to conclusions. Radsma, who measured the blood-pressure in forty persons between 20 and 30 years of age, obtained an average value of 110 mm. mercury for the systolic pressure. The American statistics give the average normal of 124 mm. for this age, and according to Halls Dally [11] the average level in England for persons between 20 and 30 years is 125 mm. Radsma recorded the blood-pressures of 12 persons within three months of their arrival in the tropics and again after two years. On an average the pressures under similar conditions had fallen 6 mm.; in two the pressures had remained the same, in all the other cases a fall had occurred. Radsma believes, however, that the number of persons examined was too small to justify the conclusion that in Europeans the blood-pressure is lower in the tropics than in temperate zones. Investigations by Knipping [13], and by Roddin and Cooper, also show that blood-pressures of Europeans fall when they are transferred to tropical climates.

I am personally convinced that in persons of all ages the blood-pressure is lower in the tropics than in Europe. This is especially so in persons with essential hypertension, in many of whom the pressure becomes normal after a residence in the tropics.

These physiological investigations have definitely shown that there

is a greater lability of the vegetative functions in tropical climates. In persons predisposed to this lability, or under the influence of detrimental factors (diseases, intoxications), tropical influences can lead to the appearance of symptoms to which the name of leiodystonia has been given. There is much to support the view that the point of attack of this tropical influence must be sought in the endocrine-autonomic apparatus. The human powers of adaptation, however, are very great. Thousands of white people can live healthily in a tropical climate, and many when they first develop symptoms of disease may recover their health even if it is somewhat labile. Only very few require a speedy return to a temperate climate to regain their health.

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Notices of Recent Publications.

A Textbook of Neuropathology. By Arthur Weil. London: Henry Kimpton. 1934. Pp. 335. Price 25s.

This book is a concise and clear exposition of the essentials of neuropathology. It pays special attention to what might be called the general pathology of the nervous system, and gives fuller accounts of the chemical composition of nervous tissue and the processes of myelin disintegration than any other book of this kind. The sections dealing with post-mortem changes and the results of fixation are of special value. The chief pathological changes in ganglion cells and the reactions of different lipoids are set out in tables, greatly to the student's convenience. There are also useful diagrams of the distribution of the cerebral arteries. Elsewhere the book follows more conventional lines. The descriptions of the different forms of cerebral and spinal disease may err on the side of brevity, but we have few other faults to find with them. The introductory remarks to several of the chapters, such as those on inflammation and intoxication, are so apposite that we regret that more has not been said on the broader pathological aspects of cerebral vascular disease and cerebral tumours.

An appendix gives useful hints on post-mortem technique and staining methods, as well as tables of brain weights in relation to age and size of head which are useful in assessing normality.

The book is illustrated with over two hundred photomicrographs, most of which are excellent.

Altogether it is a valuable little book of which the only criticism we would make is that undue stress is laid on paralysis of the vascular nerves as a possible cause of lesions of the nervous parenchyma in such different conditions as carbon monoxide poisoning and concussion of the spinal cord. The results of total ablation of the vascular efferent nerves in animals seem to be wholly against such a theory.

Neuropathology. By Walter Freeman. Philadelphia and London: W. B. Saunders Company. 1933. Pp. 349. Price 25s.

In this volume the author deals with the subject of neuropathology chiefly from the histological standpoint, and within this field he has given us a well-informed and reasonably full account of the subject. But the neglect of more theoretical sides of the subject, such as the pathogenesis of disease and the causation of symptoms, robs the book of much of the interest which the subject should have for neurologists. Only about 20 pages are devoted to diseases of

the spinal cord. No doubt its simpler structure makes long descriptions unnecessary, but this does not wholly explain the very small space devoted to it. Thus vascular diseases and tumours of the spinal cord are scarcely mentioned, and the spinal lesions of acute disseminated encephalomyelitis and rabies are completely omitted from the survey of these diseases. More attention might also have been devoted to the naked-eye appearances of tumours of the brain and to the mechanism of intracranial pressure.

In several of the sections, on the other hand, the book reaches a high level. This is especially the case where the author describes diseases of which he has made a special study, such as syphilis of the brain, torular infections and intoxications. The extent of the subject is shown by the large textbooks on it which have recently appeared in Germany, and in a book of moderate size, of which a large part is devoted to illustrations, certain sections have to be reduced to the minimum. The book appears to be of chief value to those who are embarking on a study of the histology of the nervous system. They will certainly find in it clear descriptions of the cytological changes which are seen in the commoner nervous diseases.

Volume jubilaire en l'honneur du Professeur G. Marinesco. Pp. 715. Bucarest: E. Marvan. 1933.

The length and diffuseness of most medical writings is a source of well justified complaint by the student and busy practitioner who tries to keep up to date in his subject, and probably no specialist suffers more in this respect than the neurologist. Week after week journals and monographs present to him papers of inordinate length, and yet there are few of them from which the intelligent reader cannot summarize what is new or important on a post card. This volume, published by his friends to celebrate the seventieth birthday of the distinguished Roumanian neurologist, Professor Marinesco, contains sixty-seven separate articles and numerous illustrations in little over 700 pages. There is scarcely an uninteresting contribution among them, and many contain original observations of value or present older subjects from new points of view. Few of the writers seem to have suffered from the conciseness necessarily imposed on them, and the volume is as a whole therefore less tedious and more readable than such collections of separate articles usually are. Its writers represent almost every country in which neurology is practised as a speciality, and it is consequently a valuable mirror of present-day tendencies.

An Introduction to the Study of the Nervous System. By E. E. Hewer and G. M. Sandes. Pp. 147. London: W. Heinemann. 1933. Second edition. Price 21s.

The second edition of this book, which originally appeared four years ago, is considerably enlarged by the inclusion of new matter, but there is otherwise little change. It contains a large number of diagrams, some admirably simple,

others unnecessarily complicated, and it has been the aim of the authors to present, with the help of these diagrams, as concisely as possible—and they frequently adopt tabular form—those elements of the anatomy and physiology of the nervous system which they consider necessary for clinical practice or for the purpose of examinations. In the latter object they may have succeeded, but it is doubtful if students of elementary medicine or those with a special interest in neurology will find this the easiest and most pleasing way to obtain some acquaintance with the structure and functions of the nervous system. The desire to omit nothing has made many of the anatomical chapters too elaborate and complicated, and owing to the method adopted the presentation of the subject is too diagrammatic and disconnected. In some instances the space might have been more usefully utilized : for instance, three whole pages are occupied with diagrams of the connections of the small ganglia which lie in the fifth and seventh nerves, but the structure of the cerebral cortex is not illustrated. The physiology of the nervous system lends itself more readily to treatment on these lines and some of the chapters, as those on the reflexes and on the autonomic system, will be useful to students who can assimilate knowledge in this concentrated form.

Multiple Sklerose und Erbanlage. von F. CURTIUS. S. 215. Leipzig : G. Thieme. 1933. Price 18 M.

This book is the result of an extensive research undertaken on the lines of modern genetic investigation into the occurrence of anomalies or disease of the nervous system among the relations of patients suffering with disseminated sclerosis. The author's own experience and the facts which he has collected from the literature of the disease indicate that the occurrence of disseminated sclerosis in two or more members of a family is less uncommon that it is generally assumed to be, but his chief thesis is that, regardless of the etiology of the disease, there are many factors which may determine its onset, the form it takes or the course it runs, and the inherited constitution of the subject is one of the most important of these. His statistical inquiries show that affections of the nervous system are more common and more severe in the relatives of those afflicted with disseminated sclerosis than in the average population, and the influence of a neuropathic constitution must therefore be considered in any discussion on its etiology or pathogenesis.

Les arachnoïdites spinales adhésives. Par DEM. PAULIAN et D. TURNESCO. Pp. 95. Paris : Masson et Cie. 1933. Price 24 fr.

The condition with which English neurologists have been familiar under the titles "Circumscribed Serous Meningitis," or "Chronic Cystic Meningitis" for the past thirty years has lately attracted much attention on the Continent, and especially in France. As its pathology is still uncertain and its symptomatology indefinite and often confused, a monograph in which our present

knowledge was critically reviewed and adequate facts collected to throw some light on its essential nature would be welcome. This volume scarcely satisfies these demands: the section on the ætiology of the disease is vague and nothing is added to the little we know of its morbid anatomy. The symptoms, which vary so much from case to case, are however carefully described and a series of plates illustrates the appearances most commonly found on the injection of lipiodol. The discussion of the indications for operation is also useful.

Behaviour Mechanism in Monkeys. By HEINRICH KLUVER. Chicago: University of Chicago Press. 1933. Pp. 387. Price 22s.

Dr. Kluver has carried out on monkeys an investigation so thorough and so critical that it may serve as a model for further research of the kind. It was done from 1926 onwards under the Behaviour Research Fund at the Institute for Juvenile Research, Chicago, and was intended to be a phenomenological study of animal behaviour. Such a biological approach to psychology is not new, but the author has extended it by the use of fresh methods and has tried to "correlate psychological mechanisms with brain mechanisms." This has not led, however, to any casual use of analogy as evidence of identity: throughout the book restraint and cautious examination of the evidence are conspicuous. The earlier part of the work is concerned with the general problem of behaviour mechanisms, and with methods and procedure; the last chapter is devoted to a discussion of the results in the light of various psychological theories and problems. Hypotheses for future work are put forward and their bearing on human psychology indicated. The author's grasp of the relevant literature is remarkable.

Comment diagnostiquer, comment traiter, les maladies mentales. Par L. NEUBERGER. Paris: Maloine. 1932. Pp. 424. Price 40fr.

This work is complementary to an earlier one by the same author on the treatment of nervous diseases. It is intended chiefly for the general practitioner, and its arrangement is very like that of the familiar handbooks in which easy means of reference and concise statement are preferred to detail and leisurely exposition. From this point of view it is admirable, but along with the customary French lucidity and precision there is the customary French lack of an index. The psychiatrist will be dissatisfied with the tabulated helps to differential diagnosis, so much more definite than the facts warrant, but he will be attracted by the insistence on constitution as the basis of the endogenous disorders, the unitary psychopathology offered for the affective psychoses, and the general sobriety of the author's approach. There is an unusual final discussion of the psychiatric fashions of the moment, which in France are mainly physiological and dualist.

Psychoanalysis and its Derivatives. By H. CRICHTON-MILLER. London: Thornton Butterworth. 1933. Pp. 256. Price 2s. 6d.

Psychoanalysis is nowadays a topic with which educated people are more or less familiar; many popular accounts, written with authority and lucidity, are available. Another book on the subject for the intelligent layman is only to be welcomed if it is more critical, more profound, or more comprehensive. It cannot be said that Dr. Crichton-Miller's book meets the first two of these requirements. It is comprehensive in that it has chapters on the doctrines of Freud, Jung and Adler, as well as the crepuscular Prinzhorn, but the psychoanalysis here presented is of a pleasing but unreal simplicity, and the criticisms are banal rather than penetrating.

The book may be regarded as a competent, though superficial, attempt to give the average man and woman a brief outline of some intricate, unfinished and all-embracing psychological theories of varying value and having little more than a historical connection with one another. This is undoubtedly a difficult task, but the author has succeeded in concealing the subtleties of the problem, and by a generous use of quotation has avoided personal colouring of the exposition. He passes over the difficulties and obscurities which vex analysts themselves, and by his disarming use of dilution and analogy, gives the reader the impression that there is very little to quarrel with in the views of any of these schools. In his last chapter he shows a confident, if vague, optimism, which foresees the sure discovery and conjunction of the valuable elements in all the warring theories. In psychoanalysis and its derivatives the good time coming seems so distant a millennium that aspirations towards it are epistemologically vicious for the psychologist, however useful the eclectic attitude may be for the psychotherapist.

Stoke Park Monographs on Mental Deficiency and other Problems of the Human Brain and Mind. No. 1. The Burden Memorial Volume. Edited by J. A. BERRY. London: Macmillan. 1933. Pp. 249. Price 10s. 6d.

It is difficult to understand for whom this book is intended; much of it is written in the style of a popular lecture, and if this were its purpose one might condone its carelessness as to fact and precise expression, its dogmatism, looseness of reasoning, tedious reiteration, and neglect of rules of scientific presentation.

The volume is explicitly called a monograph, but it is made up of contributions, representing "original research, study and thought," and "contributions to mental science." The customary scientific standards should therefore be applicable.

The main thesis of the book is the alleged structural changes in mental deficiency in the cerebral cortex, though no adequate histological evidence of this is furnished, and its relation to crude cranial capacity. Dr. Berry develops

these points with much repetition of elementary anatomy, expression of personal convictions, and a vigorous use of the paralogism: his papers and those of which he is part-author constitute more than two-thirds of the present volume. Some of the contributions are trivial, as photographs of defectives; others are clinical reports with didactic or diagnostic commentaries. Otherwise the most interesting features of the book are the reports of the clinical findings in 162 adult feeble-minded women, and some psychologically ambitious but uncritical tests. There is a curious bibliography which, like the text, suggests the scrappiness of the contributors' equipment for dealing with problems that are neither simple, nor new, nor universally neglected.

Fluctuations in Human Output. By S. J. F. PHILPOTT. Cambridge: University Press. 1932. Pp. 125. Price 12s. 6d.

This paper appears to have more to do with mathematics than with psychology. The main purpose of the study was to discover whether curves of output, obtained from uninterrupted mental work, are essentially periodic, the waves being geometric in nature, i.e., of constant periods when plotted against the log of time. The findings indicated that this was so and also that there was a unit of logarithmic wave-lengths that seemed to be the same for all the subjects under all the conditions of experiments met with. There is nothing in the paper but its conclusions likely to be of interest to the medical reader.

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A JOURNAL OF NEUROLOGY,

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EDITOR.